CARTRIDGE+

ROHAN SANDEEP REGE

INTEGRATED PRODUCT DESIGN

FACULTY OF INDUSTRIAL DESIGN ENGINEERING

DELFT UNIVERSITY OF TECHNOLOGY

CHAIR

Dr.ir. ARJEN JANSEN

SUSTAINABLE DESIGN ENGINEERING

MENTOR

Dr.ir. VIBHAS MISHRA

SUSTAINABLE DESIGN ENGINEERING

MENTOR - DOSER B.V.

Ir. TESSA NIJENHUIS

PRODUCT ENGINEERING AT DOSER

MSC. THESIS

AUGUST 2024

Reading Guide

This report can be navigated through two primary methods. The first method involves a comprehensive review of all provided information, encompassing sections on the project context, the research and deep dives for concept development.

Alternatively, for readers who prefer a more concise approach, a summary of key insights is available at the conclusion of each section.These summaries efficiently convey the essential information necessary for understanding the final product design and evaluation sections of the report

Use of Assistant Tools

Digital assistants are essential in any professional's tool kit, and this report benefited from three such tools: Chat GPT, Grammarly, and Microsoft Copilot.

Grammarly (without AI assistance) was instrumental in enhancing the legibility and clarity of my writing. It ensured that my communication was clear and professional.

Chat GPT provided brief insights through conversations on various topics, saving time I would have spent on extensive Googling. It also assisted in research by formulating relevant and valuable questions for experts. These tools were utilized as collaborators rather than generators, with all outputs verified to the best of my ability.

Additionally, Microsoft Copilot was used as an image generator to aid in creative sessions. While generating images in the style of specific artists helped users immerse themselves more deeply into the sessions, the ethical considerations of using these images were concerning. As a result, I used them only when absolutely necessary.

0.1 | Motivation

Over the past couple of decades, I've noticed a frustrating pattern with prescribed medicines. My doctors often warn, "This medicine is too strong for you, so take a day off." I always wondered why they couldn't just give me a smaller dose.

My mother, who suffers from motion sickness, is always asleep when traveling, even after taking just a quarter of her tablet. Splitting a small tablet less than 10mm in diameter into four equal pieces is nearly impossible, yet she's been doing it because no better solution exists.

Many old people face a similar struggle with their medications. They have to take numerous pills at different times each day, making it almost impossible to keep track of everything.

Surely, I thought, these problems only affected a small portion of the population, else we would already have solutions, but I was wrong.

This realisation became clear while working on my thesis. Whenever I mentioned 3D-printed medicine, everyone shared stories of their own medication struggles.

Though my thesis isn't the ultimate solution, it is an attempt to bring us closer to the future where everyone has access to personalised medicines. In this thesis, I introduce a concept that helps improve the efficiency of producing medicines.

Enjoy your read!
Rohan Rege

0.2 | Acknowledgements

As I reflect on this remarkable journey, I'm overwhelmed with gratitude for the extraordinary individuals who have shaped my path.

Arjen, my chair, your unwavering support and openness have been truly inspiring. Your knack for finding solutions in every situation consistently left me feeling hopeful and motivated after our meetings. Vibhas, your silent trust and casual conversations were a welcome relief, while your thought-provoking questions pushed me to deeper reflection and personal growth.

Tessa, I cannot thank you enough for your open-mindedness as my company mentor. Despite my significant deviations from the original assignment, your steadfast support and encouragement to explore have been invaluable. Your trust in my vision has touched me deeply.

To the Pharma Team at Doser and our clients, I'm profoundly grateful for your trust and for welcoming me into your circle. Fereshteh, a special thank you for challenging me to reach new heights and supporting me through the low points.

Wolf, I'm immensely thankful for the opportunity to work with you. Our enlightening conversations, your generous mentorship, and yes, the coffee, have all been integral to my journey.

Finally, to my beloved mother, words cannot express my gratitude for your unconditional love and incredible sacrifice. You gave me the luxury to quit my job and pursue this master's degree. This dream would not have been possible without you. Your unwavering support has been the foundation of everything I've achieved.

To each of you, and to the countless others who have supported me along the way, thank you for being part of this transformative experience. Your contributions have been invaluable, and I will carry the lessons learned from each of you throughout my future endeavors.

This thesis introduces the 'Cartridge+ Ecosystem' concept, enhancing Doser's current tablet 3D printer. This innovation reduces tablet printing time from 25 to 6 hours and reduces manual oversight.

The design aims to help Doser in their goal to enable pharmacists to produce personalised medication on demand more efficiently.

0.3.1 | A More Efficient Printing Process

Doser established in 2019, is a pharmaceutical device manufacturing company specialising in the Rx1, a tablet 3D printer.

Although used by customers, the printer (Fig. 0.4) is still under development. Hence the printing process (Fig. 0.1) has potential for optimisation. This report analyses the current process in detail, deconstructing it into smaller components and addressing each one individually to propose an improved process (Fig. 0.2). I propose a new concept based on these enhancements.

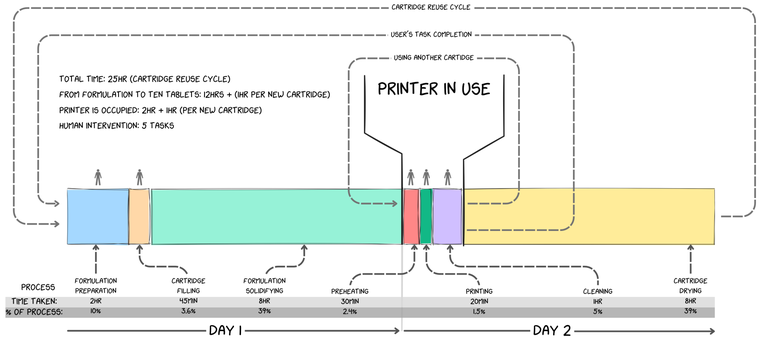


Figure 0.1 Old Process

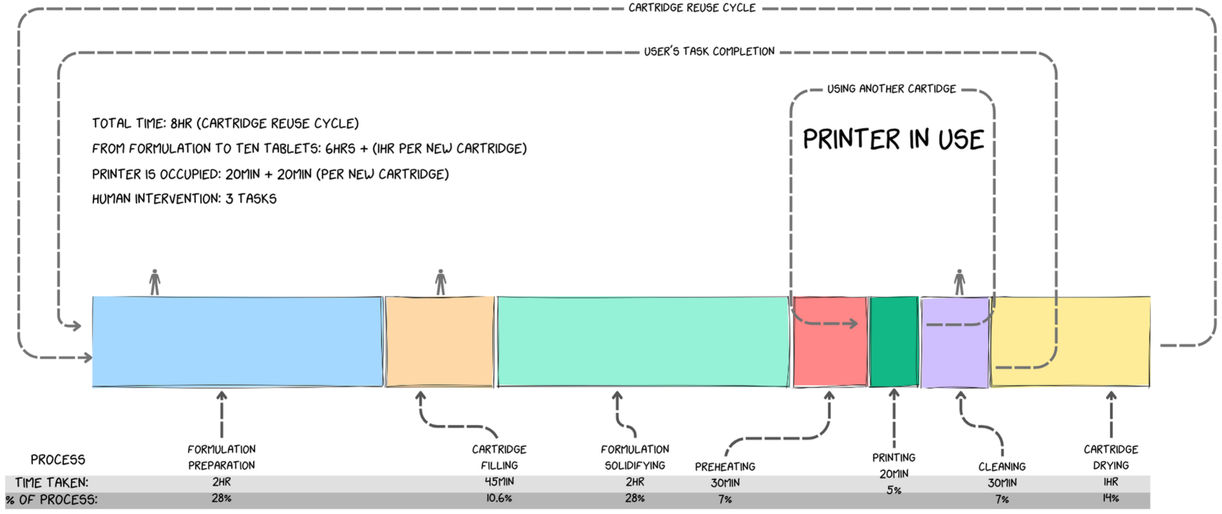


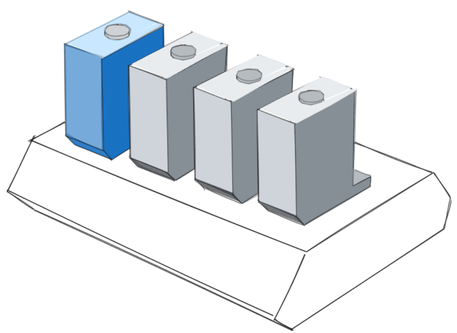
Figure 0.2 Old Process

0.3.2 | Cartridge Plus Ecosystem

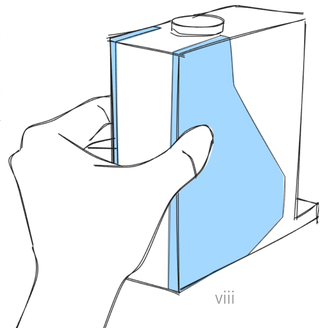
The cartridge and ecosystem (Fig. 0.3) consists of three elements: A cartridge, a print head and a base station. This ecosystem enables users to remotely control and monitor consumables, track the status of each cartridge, and organise and queue print jobs.

Each cartridge is equipped to store the formulation name, track the formulation status, measure the remaining quantity, and predict when it will be ready for printing.

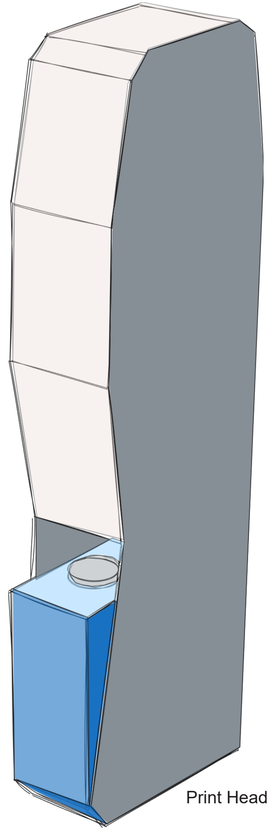
This information is displayed on a dashboard, facilitating efficient planning for users. By analysing formulation usage, users can also accurately estimate when to prepare or order new formulations.



Base Station



Cartridge Plus



Print Head

Figure 0.3 Eco System

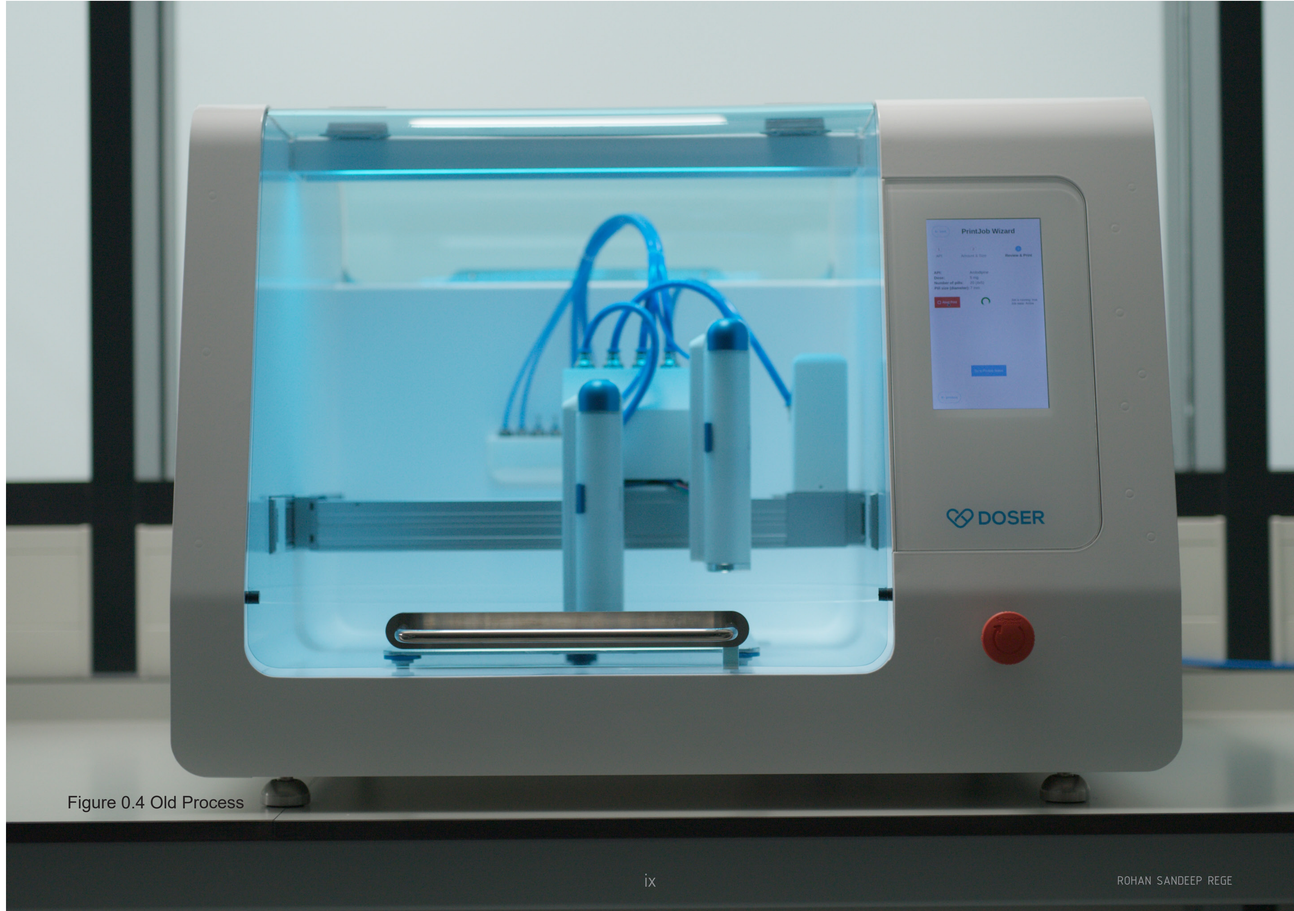


Figure 0.4 Old Process

Figure 0.5 Cartridge Plus

0.3.3 | Cartridge Plus

The cartridge plus (Fig. 0.5) is at the core of the new ecosystem. Since the printer's main task is to print tablets, I propse the decouple other tasks such as preheating, solification from it.

Each cartridge plus is equipped with a heating and cooling module, a memory module and a display to visually indicate the current status of the formulation.

The enables the cartridge to force cool and hea the formulation reducing the cycle time. The cartridge plus, is tracked and controlled by placing on the basestation or in the printer.

0.3.4 | New Print Head

The new print head (Fig. 0.6) is a simplified version based on the current design. Unlike its predecessor, the print head is now solely responsible for extruding the tablets.

Additionally, the print head, in conjunction with the printer, registers new formulations and cartridges.

The printer also calculates the remaining formulation by assessing the position of the plunger and analysing previous print logs. This information is relayed to the dashboard and shared with the cartridge via the print head, indicating the remaining amount of formulation.

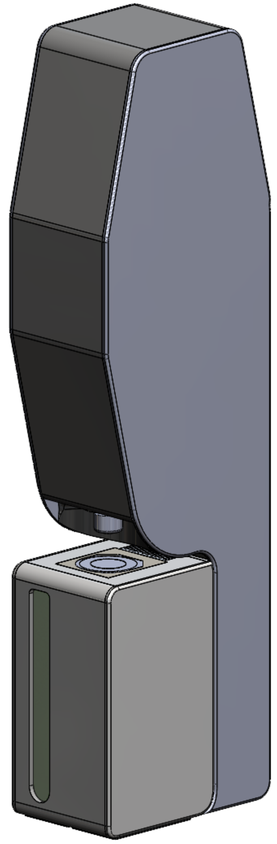


Figure 0.6 Print Head

0.3.5 | Base Station

The base station (Fig. 0.7) is a new addition to the current product portfolio. The base station ensures that all formulations are always ready for printing.

It also facilitates the ex situ heating and cooling of formulations, allowing multiple formulations to be controlled and maintained in a print-ready state.

Additionally, like the print head, the base station can also be used to register new formulations.

The new user flow of the process is illustrated on the next page Fig 0.9

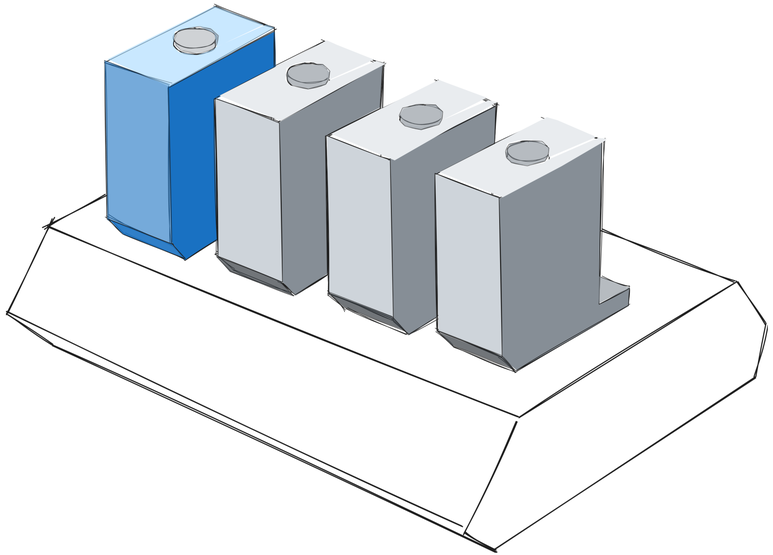


Figure 0.7 Base Station

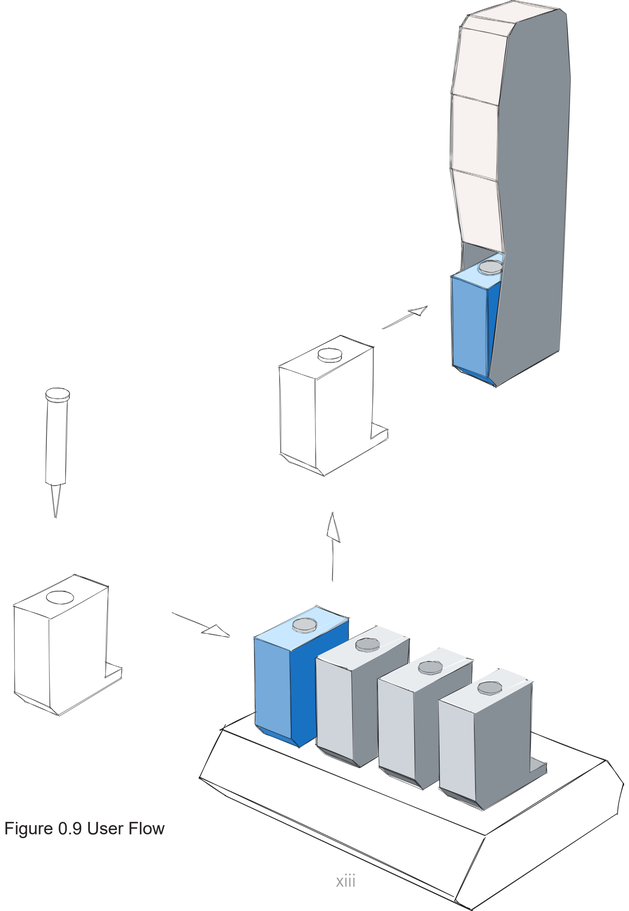


Figure 0.9 User Flow

Table of Contents

1. Introduction 1
2. Research 9
3. Field Studies and Interviews 38
4. Design Requirements 64
5. Ideation 72
6. Cartridge Plus Ecosystem 76
7. Evaluation 86
8. Conclusion 97
9. References 101

1. Introduction

1.0 Preface

A Tour de France cyclist would not choose the same bike as a teenager, yet both might rely on the same generic paracetamol tablet when ill. This highlights a critical issue in healthcare: despite the significant differences in individual needs, medications often adhere to a ‘one-size-fits-all’ approach, neglecting the unique requirements of each patient

In North America and Europe, over 75% of pediatric prescriptions are ‘off-label,’ meaning children receive medications that have not been tested explicitly for their age group (Rieder, 2019). This underscores a broader issue in personalised medicine, where many patients lack access to customised treatments tailored to their individual needs.

Currently, the production of personalised medicine is labour-intensive and time-consuming, involving numerous verification steps to ensure compliance and stability. This limits personalised treatments primarily to sensitive populations and constrains the broader application of personalised medicine

The advent of robotics and automation is beginning to address these challenges. By incorporating advanced technologies, such as Doser’s Rx1, a robotic 3D printer, the pharmaceutical manufacturing process is evolving. The Rx1 utilises semi-solid extrusion (SSE) technology to produce customised tablets on-site and on-demand, offering a scalable solution to the limitations of traditional methods. This system reduces the need for manual labour, enhances precision, and minimises the risk of human error (Javaid et al., 2021).

The Cartridge Plus ecosystem further complements this innovation by providing an automated, modular approach to cartridge refilling, thus improving efficiency and sustainability in personalised medication production. By integrating these technologies, this project aims to transform the production of personalised medicine, making it more accessible, efficient, and reliable for a broader range of patients. In essence, this project represents a significant step toward redefining pharmaceutical manufacturing, aligning it more closely with individual patient needs and advancing the field of personalised medicine.

IT IS MORE IMPORTANT TO KNOW WHAT SORT OF PERSON HAS A DISEASE

THAN TO KNOW WHAT SORT OF DISEASE A PERSON HAS.

HIPPOCRATES

1.1 Context

This is a graduation project for a master's in Industrial Design Engineering at the Delft University of Technology.

Doser is a Dutch company making equipment for the 3D printing of medicines. As a start-up, Doser is constantly looking to improve their product services. And stay attractive to their clients

To help them, I propose 'Cartridge Plus'. A concept that could enable pharmacies to print tablets in six hours and sent to the patient.

Throughout this graduation project, my main contact was Tessa Nijenhuis, Product Engineering at Doser. I also had the opportunity to visit and work from Doser's offices at PLNT in Leiden.

Doser also provided me access to their clients for me to interview and evaluate my concepts.

Figure 1 Doser Logo

1.2 Problem Statement

1.2.1 From Proof-of-Concept to a Product

Previously, Doser concentrated on validating their technique and developing prototypes of their device using existing FDM 3D printers.

Having proven the viability of their method, Doser launched Rx1, a commercially reliable printer for the market.

This shift opens an opportunity to prioritise user experience by seamlessly integrating the printer into pharmacists' and researchers' existing and envisioned work-flows.

1.2.2 Need for Higher Throughput

The tablet printing process is still in development, leaving room for optimisation. It's time-consuming, involving multiple steps of heating, solidifying, and reheating the material to precise temperatures.

These inefficiencies causes the printer to fall short of users' expectations.

1.2.3 Need for more scientific evidence

Doser needs clarity on the necessary heating duration before the formulation is ready for printing.

Furthermore, not much information is available

on whether the formulations can be reused or can be thermally stressed to fast track the printing process.

These reasons lead to the following initial problem statement:

The prolonged heating and cooling cycle time of cartridges in Rx1 hamper its throughput, causing delays in production and inconveniencing end users.

In this project, I examine the existing printer, competing devices, product context, users, and intended printer usage in this project.

The goal is to advance personalised drug manufacturing, addressing the requirements of researchers and compounders in academic and pharmacy settings while enhancing overall efficiency.

Refer appendix A for the original project brief.

1.3 Scope

This graduation project proposes optimizations to the current formulation preparation process. The key proposal is to rapidly solidify the liquid formulation and then maintain it at the required temperature. This approach reduces the time needed to transition from pouring the formulation to printing the tablets, while ensuring the stability of the medical ingredients.

The primary focus on this graduation project is on improving the efficiencies of the process

Final Deliverable(s)
- The New Printing Process
- The Cartridge Plus Design Concept
- The New Print Head Concept
- The Base Station Design Concept

To advance the personalised drug manufacturing, addressing the requirements of researchers and compounders in academic and commercial settings

Design Goal

1.4 Approach and Methods

Given the complex nature of this project, a step-by-step approach was used to break down the problem. The project was split into smaller parts, each representing a separate design problem, to handle the overall complexity more easily.

The double diamond approach was used for each part, providing a clear framework for problem-solving. This approach was improved by using the Integrated Creative Problem Solving method (van Boeijen et al., 2014), which helped to organise each problem and guide the solution process.

Getting stakeholders involved was a key focus throughout the process. Ideas from Creative Facilitation (Tassoul, 2009) and Integrated Creative Problem Solving (Boom, 2019) were used to involve both current and future stakeholders. This helped to make the problem statements more relevant and increase the likelihood of proposed solutions being accepted.

The process used was flexible and not always in a straight line. Many steps were often worked on at the same time, with frequent returns to earlier stages when needed. Sometimes, certain paths or parts were either dropped or combined with others as the project moved forward, based on new research findings.

Finally, the proposed solutions were integrated into a final design concept.

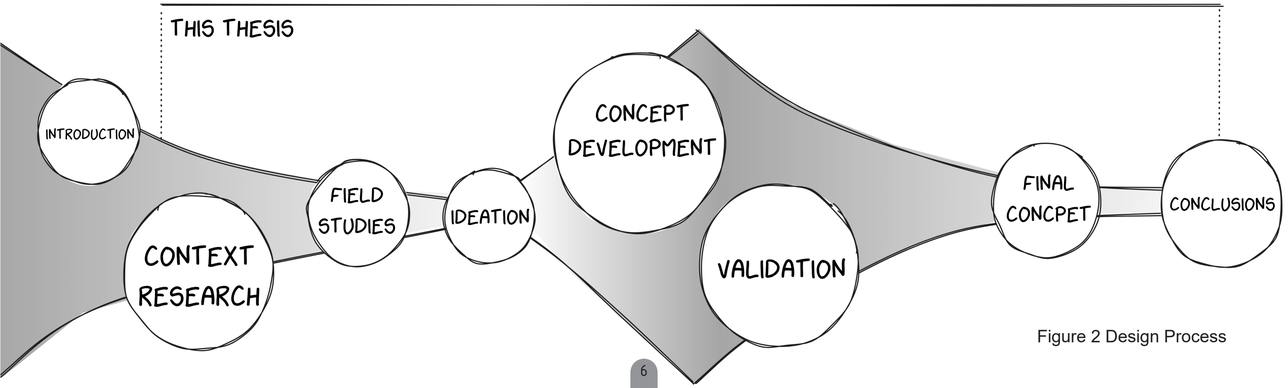


Figure 2 Design Process

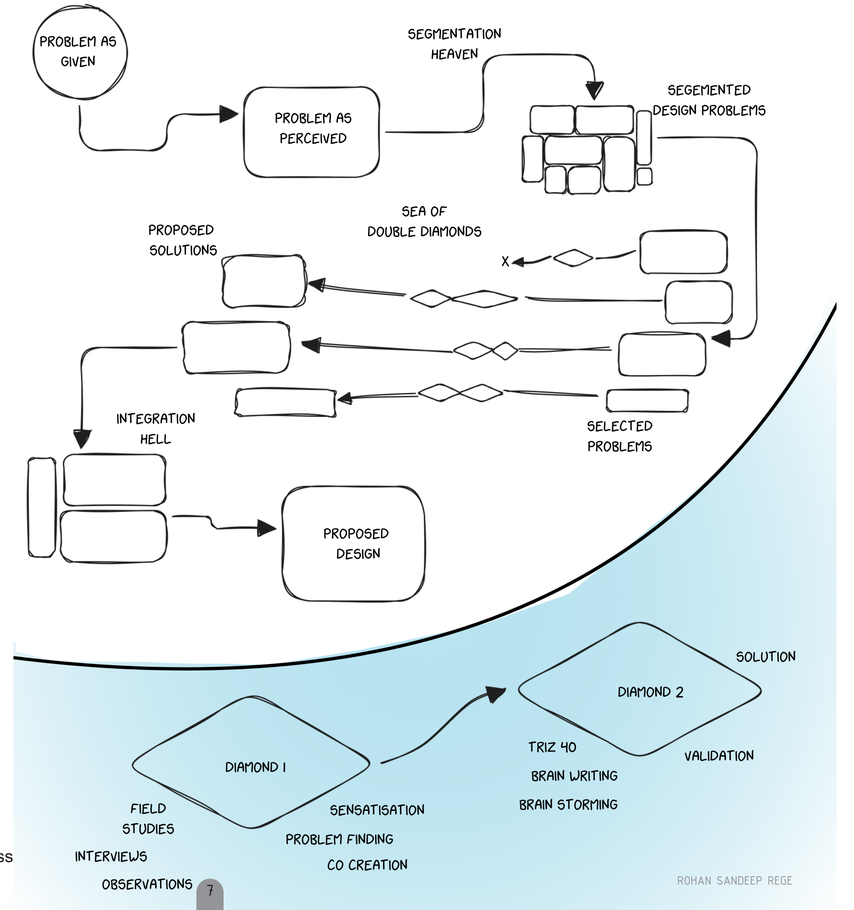


Figure 3 Personalised Design Process

2. Research

2.1 Market for Personalised Medicines

The pharmaceutical market in Europe has been developing rapidly in recent years, with several trends and developments shaping the industry.

The projected revenue in the pharmaceuticals market is estimated to reach €1,071.00 billion in 2024 and is projected to grow at a CAGR of 4.94% from 2024 to 2030, while the subsector of personalised medicine sector is expected to grow at a rate of 8.20%. (Statista, n.d.)

In Europe, customers are increasingly demanding personalised medicines that are tailored to their specific needs. This trend is driven by technological advancements, which allow for more precise diagnosis and treatment of diseases. (Precedence Research, n.d.)

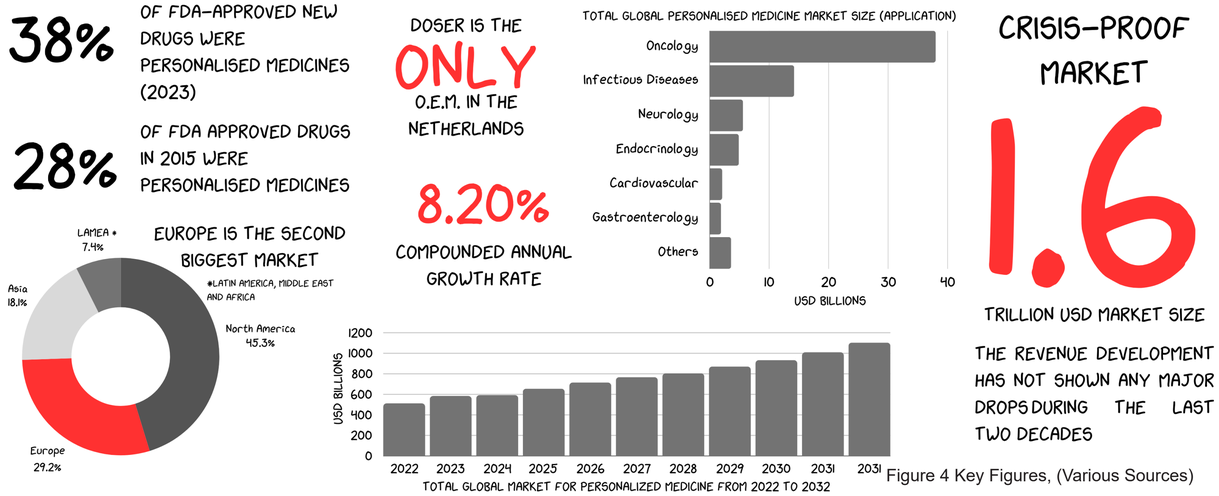


Figure 4 Key Figures, (Various Sources)

2.2 Competitor Analysis

This chapter analyses how Rx1 compares with similar market offerings to establish benchmarks and understand its competitive position.

In the desktop tablet printer segment, Doser competes with FabRx, Cellink, Goatam, CurifyLabs and DiHeSys. (Fig. 5)

A spec-by-spec comparison reveals that the FabRx M3DIMAKER 2 is remarkably similar to the Rx1. Both printers feature multiple print heads, achieve comparable temperatures, have similar build areas and are specifically designed for tabletting.

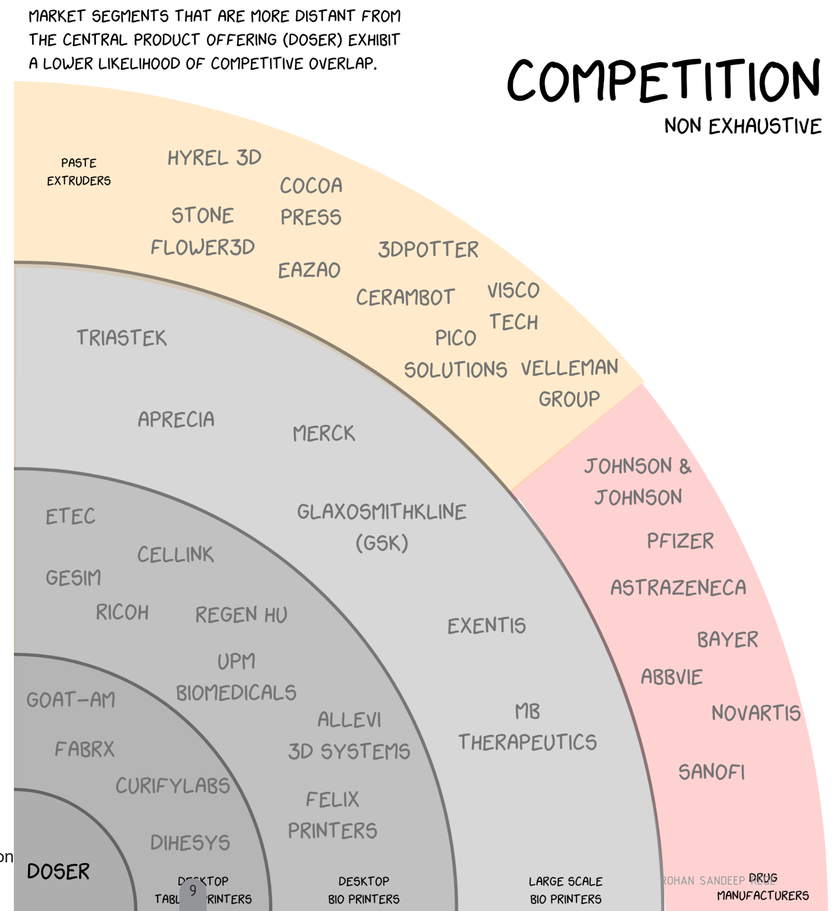


Figure 5 Competition

Doser's current commercial portfolio is focused primarily on semisolid extruders (paste extruders). Doser offers a significant advantage with its multiple printheads that support a higher 40ml cartridge capacity of more than twice that of any other competitor. On the other hand, FabRx provides an interchangeable printhead system that accommodates a broader range of technologies (Fig. 6).

Furthermore, FabRx also provides a software suite to control the printer and hardware 'upgrades' such as a near IR sensor, Pressure Sensor, Balance and UV Led System. FabRx is the only player providing these features in this product segment.

To Doser's advantage, they are the only manufacturer providing reusable metal cartridges. In the future, they plan to **(refer confidential appendix section 2.2)**

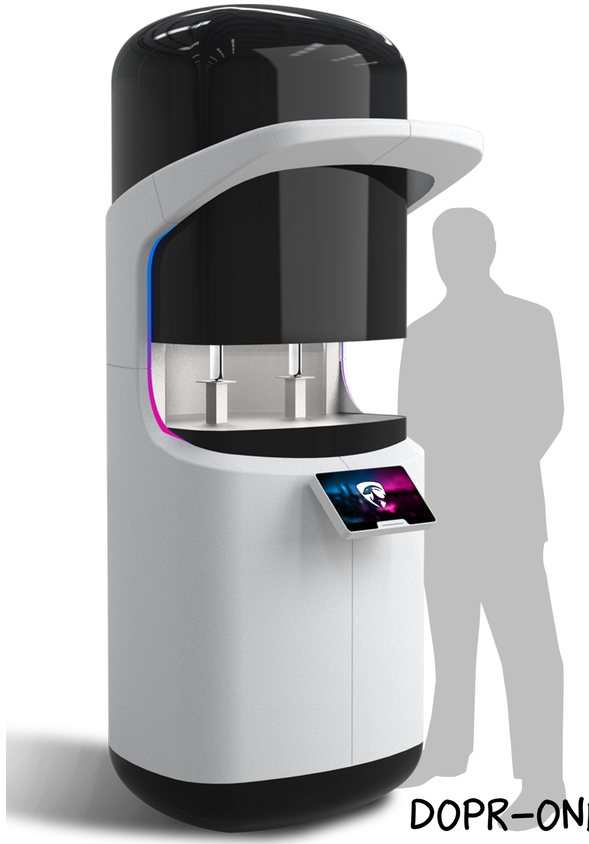
Using metal cartridges also enables Doser to provide safer heating at higher temperatures. Looking at the future and possible regulations shaping the industry (more in section 2.4.2), having a reusable cartridge system over a single-use disposable one enables Doser and its clients to be better prepared to comply with the regulations.

According to published product specifications and visual materials, Doser is the only one that provides a metal print plate, which can be regarded as being better in terms of cleanability and durability.

TNO, a nonprofit, also has similar technology available for licensing.

Companies like Trianstek and Aprecia are developing technologies aimed at high-volume 3D printing for large-scale tablet printers but have yet to commercialise their offerings fully.
In the 3D bioprinting category, competitors utilise technology akin to Doser's, primarily marketing their devices as plotters. These companies could potentially shift into Doser's market segment.

Lastly, paste extruders share core technology with 3D bioprinters but are less sophisticated and would require considerable adaptation to compete directly with Doser.



M3DIMAKER2

FABRX

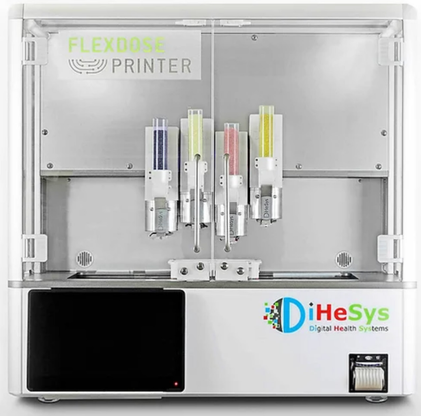
MEDIMAKER PRINT HEADS

SSE

FDM

POWDER DEPOSTION

Figure 6 Competition - II



DIHESYS

CELLINK

CURIFY LABS

PHARMACEUTICAL 3D PRINTER SPECS

	PRINTHEADS	REUSEABLE CARTRIDGES	FORMULATION LIBRARY	CARTRIDGE VOLUME	HEATING MAX. TEMP	COOLING MIN. TEMP	PRINTER SOFTWARE
 DOSER RXI	2	Y	Y	40 ML 7 ML	Y_{85}	N	Y
 FABRX MEDPRINT 2	2	N	Y	20 ML	Y_{100}	N	Y
 CELLINK INKREDIBLE+	2	N	N	20 ML	Y_{130}	N	Y
 GESIM BIOSCAFFOLDER	3	N	N	10 ML 1.5 ML	Y_{190}	Y_{4}	Y
 REGEN HU R-GEN 100	5	N	N	-	Y_{40}	N	Y

Figure 7 Competition - iii

Key Takeaways

1. The 3D compounding market is still emerging and developing.
2. FabRx and Doser both have very similar offerings, with FabRx having a slighty more bigger portfolio, but Doser has a smaller but more mature product
3. All the companies (including Doser) are secretive of their work, with no videos of the technology and working of all the products in their portfolio.
4. Doser the only equipment manufacturer in the Netherlands.

2.3 Stakeholder Analysis

The stakeholder map Fig. 8 for the personalised medicine market depicts the interests and level of influence of stakeholders. The arrows illustrate the influence of stakeholders on each other, except for those of regulators (government) who impact each stakeholder through new regulations. While the placement of each stakeholder on the map is based on estimates, it provides valuable insights into the market's dynamics.

While Doser is actively developing equipment for printing medicines, it currently operates as an Original Equipment Manufacturer (OEM) and does not possess the necessary licenses to manufacture or distribute pharmaceutical products directly.

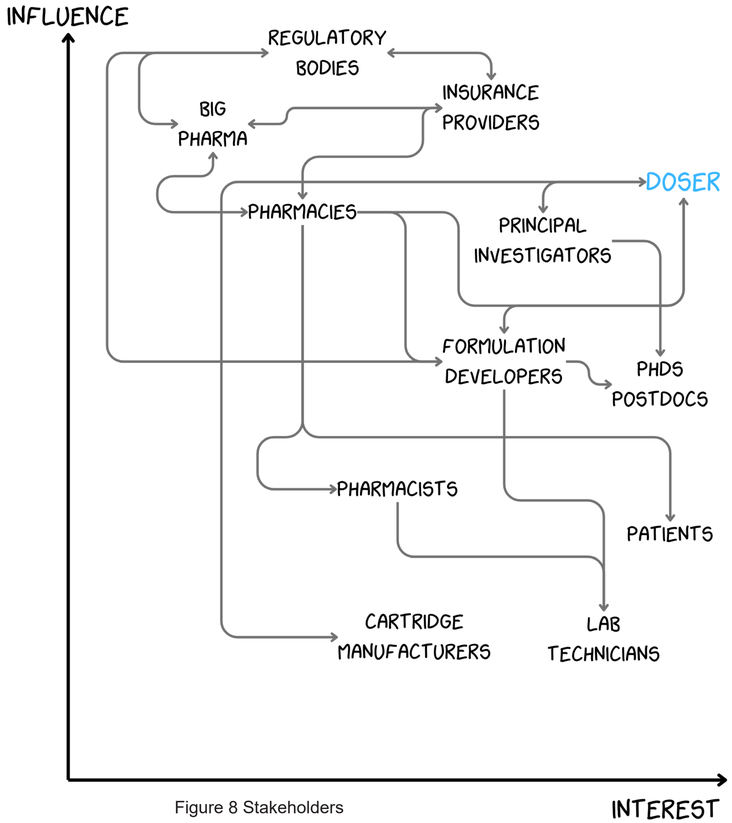


Figure 8 Stakeholders

Doser's device's uptake largely depends upon pharmacy engagement, positioning pharmacies as critical stakeholders in the market. Additionally, researchers conduct much of the developmental work under the influence of the principal investigators, rendering them another significant cohort in the market landscape.
It is critical to note that though the pharmacies and principal investigators have high influence, their interest is split between Doser, its competitors and other competing technologies in the 3D printing tabletting field.

To address this limitation, Doser has established strategic partnerships with various pharmacies and university hospitals to facilitate the development and future use of bespoke medicines. These collaborations are crucial for the adoption and implementation of Doser's technology.

For smaller pharmacies, which constitute a substantial portion of Doser's client base, a similar ethos of growth through collaboration is observed. This collaborative approach appears to be a defining characteristic of the market's development strategy.

The patients, pharmacists, and lab technicians are hopeful that the product will alleviate their quality of life. Have no significant influence as most decisions are made for them.

Key Takeaways

1. The adoption of Doser's 3D printer is highly dependent on stakeholders.
2. To develop a solution, the PhDs, and Pharmacists (End Users) need to be involved.

2.4 Regulations and Norms

2.4.1 Current Regulations and Norms

The EU Medical Device Regulation (MDR) defines medical devices as any instrument, apparatus, implement, machine, appliance, implant, or reagent for in vitro use, intended by the manufacturer to be used alone or in combination for a medical purpose.(EUR LEX - 02017R0745-20240709, 2024) Since Doser's Rx1 does not meet these criteria, it is not classified as a medical device. Instead, the printer is considered a pharmaceutical device.

Pharmaceutical devices are regulated by various governmental agencies, such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA). This ensures their safety and effectiveness. To meet these regulations, manufacturers must comply with various standards and guidelines for design, manufacturing, and testing, (Richter, 2011). Additionally, regulations and norms for pharmaceutical devices may vary by country and region. Manufacturers must adhere to the guidelines of the countries where they plan to market the device.

Two important international standards for developing and producing pharmaceutical devices are ISO 9001 and ISO 13485 and Good Manufacturing Practices (GMPs).

Thus far, no regulatory body has issued guidelines for 3D-printed preparations. I believe that as the technology continues to mature and researchers continue to explore, regulators can establish a set of scientific standards in the pharmaceutical field.

In a non-industry specific area, the EU has the CE mark and WEEE mark.

CE marking indicates that a product has been assessed by the manufacturer and deemed to meet EU safety, health and environmental protection requirements Unlike standards the mark does not indicate quality or certification The European Union sets of guidelines for the CE mark. Many products require CE marking before they can be sold in the EU. It is required for products manufactured anywhere in the world that are then marketed in the EU. (CE Marking, n.d.) For products like the pharmcetiacal 3D printer, and independent assesment might necessary to have the CE mark on the product.

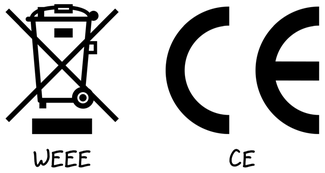


Figure 9 WEEE, CE

For Doser, another required mark is that of the WEEE. The symbol indicates that the product should not be discarded as unsorted waste but must be sent to separate collection facilities for recovery and recycling. The WEEE marking must appear on any electrical and electronic equipment placed on the EU market. (WEEE, n.d.)

2.4.2 Potential Norms and Regulations Shaping the Future

In more industry-specific areas, all medical formulations, their directions for use and side effects are documented in the pharmacopoeias. Every country (or a union of countries) has a published pharmacopoeia. While Doser is not a drug manufacturer, at this stage they're collaborating with multiple stakeholders to develop (or modify) the formulations to work with the Rx1. It is not yet clear if modifications to existing medicines require regulatory approvals.

Compared to conventional products, Doser's offering is that of a product service. Akin to

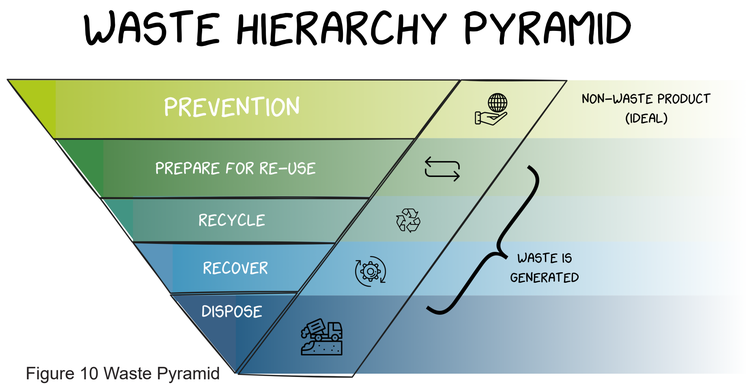


Figure 10 Waste Pyramid

Xerox charging per print rather than selling the printer, Doser plans to charge per tablet printed instead of selling the printer as the product, while providing service and maintenance for the printer. Making Doser's client free print whatever they want on the machine.

From an industry-agnostic view, the European Union's Green Deal initiative aims to promote sustainable practices and reduce the environmental impact of various industries. To achieve this goal, the EU has implemented various legislation, such as the Sustainable Products Initiative (European Commission, 2020), Extended Producer Responsibility (European Commission, 2014), the Plastic Tax (WTS Global, 2022), and the Waste Framework Directive (European Commission, n.d.). The Waste Framework Directive establishes a hierarchy of waste management options, prioritising waste reduction and reuse (Fig. 10).

Although current sustainability regulations do not directly apply to companies like Doser, they should proactively design sustainable products in anticipation of future regulations. S. Rieder and T. Koch from Rytec Circular created a "worst-case scenario" for current single-use devices (Fig. 11). This scenario highlights potential upcoming regulatory, economic, and societal pressures that could compel pharmaceutical companies to adopt more sustainable practices.
Doser holds a distinct advantage over its competitors by utilising reusable metal cartridges instead of disposable plastic ones. Doser's printer and its product line are specifically designed to be compatible with these metal cartridges. For competitors to transition from plastic to stainless steel cartridges, they would need to make significant investments and efforts in the future.

As the first and only OEM to offer stainless steel cartridges, Doser benefits from a first-mover advantage. This could potentially lead to these cartridges becoming the industry standard, similar to how Tesla's EV chargers have been widely adopted and mandated since 2023. (J3400: NACS - SAE International, n.d.)

Key Takeaways

1. ISO provide strict norms for testing and quality management. These are not considered in this project's concept design but should be considered in a later development stage.
2. Although no drug-related regulations apply directly to Doser, they must consider them while developing the products.
3. Doser is better prepared than the competition to comply with the regulations.

Figure 11 Single use products

WORST CASE SCENARIO

FOR SINGLE USE PRODUCTS WITH DEVICE

Risks	Timeline 2023	2035	2050
Legislative 	• Ongoing exceptions regarding CE and environmental requirements in different legislations for infectious medical devices and medicinal products with device component. • Eco Modulation for secondary packaging	• Prohibitions of substances • Collection, label, and recycling requirements • No exceptions for medical devices. Infectious parts must be separated. • Exceptions for medicinal products with device component only, if sustainable solutions are technically impossible. • Eco Modulation for products (costs). • Eco Modulation for primary and secondary packaging (costs).	• Prohibition of existing unsustainable products • No exceptions if technically possible (burden of proof) • Extensive eco-design requirements (refill, reuse, material, separable, recycling, etc.)
Economic 	• Competitor companies are ready for Circular Economy • They use economic advantage of CE (lower production costs through reuse of product, components, material)	• Reputation risk • Competitors are outperforming industry standards • Products of competitors are better with better prices (TOC) • Shortage of sustainable material on the market. Competitors have established contracts with better prices.	• Loss of profit • Loss of market share
Societal 	• Status quo	• Zero acceptance for single-use products	• Well-educated society regarding sustainable products

2.5 Commercial Tabletting Process

Commercial tabletting has existed since the 19th century, and today, the manufacturing is almost perfected. Commercial-grade machines can make upwards of 30,000 tablets per hour. (Piccola Tablet Press – Riva Europe, n.d.)

The first tablet-making device was patented by William Brockedon in 1843, who is credited as the inventor of the compressed tablet. (Tools of the Trade | RPS, n.d.)

The tablet comprises a mixture of active substances also known as the active pharmaceutical ingredient (API) and excipients, usually in powder form. Excipients are pharmacologically inert ingredients added intentionally to a tablet for various functional roles, such as to enhance dosage form, volume or size, disintegration of solid dosage forms, binding of particulates, lubrication during processing, taste masking, or modifying drug release. (Developing Solid Oral Dosage Forms, 2017)

APIs typically are complex molecules, while excipients are simple, long-chain polymers for stability.

For example, an OTC (over-the-counter) Paracetamol 500 tablet contains paracetamol (API) with a molecular weight of 151.1 g/mol. In comparison, gelatin (excipient) ranges from 20,000 g/mol to 100,000 g/mol, depending on the chain length. (Geneesmiddeleninformatiebank, n.d.).

Most tablets are made by compacting the API and excipient. Compression involves particle

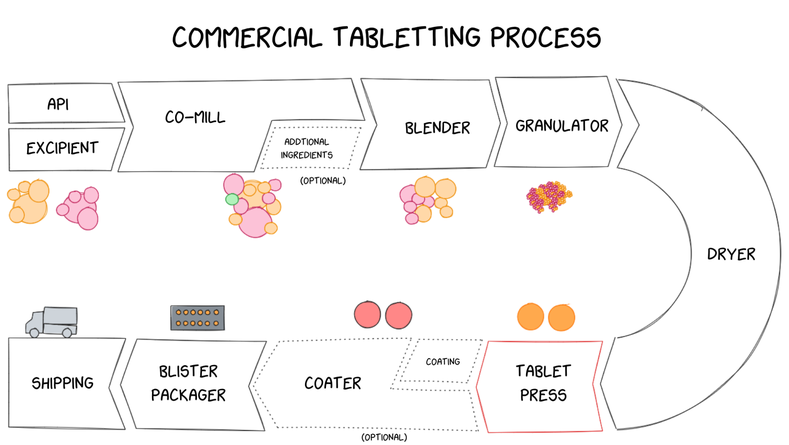
	COMMERCIAL TABLETTING	COMPOUNDING	3D COMPOUNDING
PRODUCTION METHOD(S)	INDUSTRIAL EQUIPMENT, AUTOMATED	SMALL SCALE PRODUCTION, USUALLY MANUAL	VERY SMALL SCALE PRODUCTION, AUTOMATED
PRODUCTION VOLUME	~518,400 TABLETS PER HOUR PER MACHINE USUALLY, MULTIPLE MACHINES RUN IN PARALLEL	~100 TABLETS PER PHARMACIST PER DAY USUALLY, MULTIPLE PATIENTS	~20 TABLETS PER HOUR USUALLY, MULTIPLE FORMULATIONS
CUSTOMISATION	NONE, DESIGNATED PRODUCTION LINES EXIST FOR SIZE, SHAPE AND FORMULATIONS	HIGH, EACH PRODUCTION RUN IS BASED ON THE PATIENT'S REQUIREMENTS.	VERY HIGH, TABLETS CAN BE VARIED WITHING THE SAME PRODUCTION RUN
REGULATORY COMPLIANCE	HIGH, STRICT ADHERENCE TO GMP AND OTHER REGULATIONS.	REGULATED BUT LESS STANDARDIZED THAN LARGE-SCALE PRODUCTION.	EVOLVING REGULATORY STANDARDS WITH SOME APPROVALS.
USE CASE(S)	MASS-MARKET DRUGS, COMMONLY USED MEDICATIONS.	SPECIAL CASES, ALLERGIES, RARE CONDITIONS, UNIQUE DOSAGES.	COMPLEX OR MULTI-DRUG THERAPIES, PATIENT-SPECIFIC TABLETS, CLINICAL TRIALS.
EXAMPLES	OVER-THE-COUNTER TABLETS, CREMES. E.G. PARACETAMOL	PAEDIATRIC DOSAGES BASED ON CHILD'S WEIGHT.	PEADIATRIC TABLETS WITH DIFFERENT SHAPES IN THE SAME BATCH
COMPANIES	GSK, BAYER, PFIZER	NEIGHBOURHOOD APOTHEEKS	DOSER, FABRX (OEMS) APOTHEEKS (MANUFACTURERS)

Figure 12 Various compounding processes

Figure 13 Tablet presses, tools of trade

ROHAN SANDEEP REGE

rearrangement, fracture, and deformation, influenced by interparticulate interactions like van der Waals forces and hydrogen bonding. As compression begins, particles rearrange and come closer, enhancing interactions. The particle nature and strength determine compression forces to prevent particle fracture. At the end of compression, particle deformation occurs, increasing interaction through majorly plastic and minor elastic deformation. Successful tabletting hinges on these interactions, material properties and compression process. (Rapaille et al., 2003)



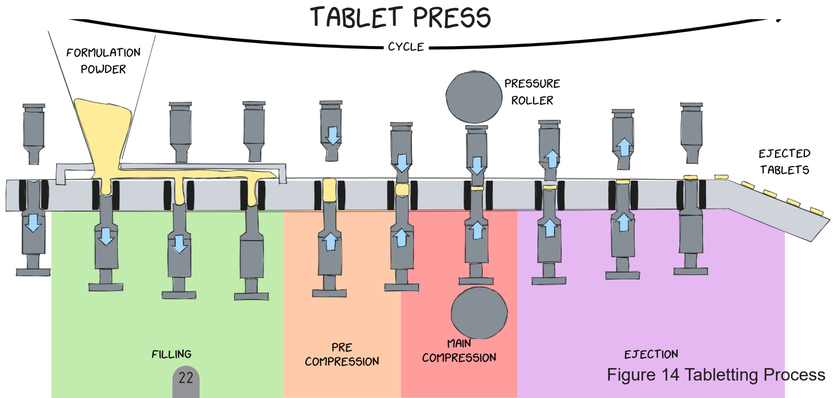


Figure 14 Tabletting Process

2.6 Compounding of Medicines

Compounding is the preparation of custom medications to fit the unique needs of patients. This is typically performed by compounding pharmacists who mix, combine, or alter ingredients to create medications that are not commercially available or to accommodate specific patient requirements such as dosage strengths, flavours, or forms. The most common form of compounding is oral suspension.

A suspension is dispersion of solids in a liquid, in chemistry a suspension is a heterogeneous mixture of a fluid that contains solid particles sufficiently large for sedimentation. The particles may be visible to the naked eye, usually must be larger than one micrometer, and will eventually settle, although the mixture is only classified as a suspension when and while the particles have not settled out. (McNaught & Wilkinson, 1997) e.g Milk

One field in which compounding is particularly common is paediatrics. Paediatric patients span a wide range of sizes and metabolic capacities, from pre-term babies to adolescents, and require a wide range of doses to meet their needs.

The process of administering personalised compounded medicines to children involves several steps. Initially, the doctor prescribes the medicine, weighs the child and performs the necessary calculations to determine the exact strength of the dosage. Subsequently, at the pharmacist independently measures the child's weight and verifies these calculations before preparing the medicine. A third verification check is conducted by quality assurance before handing over the medicine to ensure safety. (Interviews)

A challenge with current personalised medicines (suspensions) is the tendency for the components to separate or settle over time, a phenomenon known as settling. As a result, these suspensions must be shaken before each administration to ensure uniform distribution. (Interviews). Hence, liquid medicines say, 'Shake well before use'. However, the amount and intensity of shaking are variable, making it difficult to guarantee a precise dose. Similarly, when using a spoon to administer the medicine, the volume may not always be accurate.
In a pharmacy, the current protocol for preparing formulations for sensitive populations

(for example, cancer patients) requires the involvement of three individuals. The first person mixes the formulation, while the second observes the process and documents it. The third person verifies both the weight and the documentation. This process is quite time-consuming and heavily reliant on human resources. Pharmacies are now developing new protocols that incorporate the use of robots in these processes. Implementing robotics provides repeatability, reduces workload, and simplifies the protocol. (Interviews)

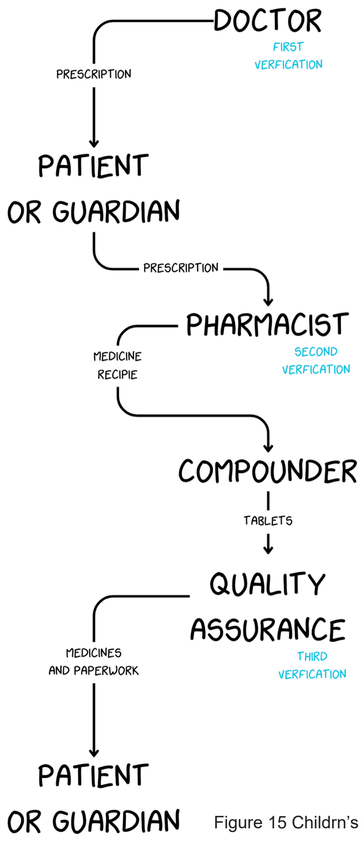


Figure 15 Childrn's Meds

2.7 3D Compounding of Tablets

Compared to commercial tablet production, an average 3D compounding machine, like the Doser's Printer, advertises 100 tablets per hour. This rate is slower than the current manual compounding process. However, the ability to customise tablet shapes and consistently achieve perfect results with minimal human intervention makes this technology appealing.

Many 3D compounding technologies are in development. These are adaptations of current additive manufacturing techniques.

The matured techniques in material extrusion are:

- BJ-3DP: Binder Jet 3D Printing is similar to inkjet printing, where binder droplets are sprayed over a powder bed to create 3D geometries.

- FDM: The Fused Deposition Modelling technology is widely used in pharmaceuticals due to the advantages of simple equipment, low cost, and high product strength.

- SSE Technology: Semi-solid extrusion is an additive manufacturing technology that deposits semisolid material layer by layer, where the extrusion head moves and extrudes; it is similar to FDM, the difference being that the material is a gel or semisolid paste.

2.9 Semi-Solid Extrusion

Like FDM, this technology also utilises material extrusion through a nozzle. Some materials require controlled heating to maintain the material state during deposition. Extrusion systems can be driven pneumatically or mechanically, each suited to specific applications.

The semi-solid nature of the material necessitates highly precise control to prevent print failures (Fig. 16). Key to successful printing is understanding the material's rheological properties, the study of the deformation and flow of materials, encompassing both solids and liquids.

Firstly, the semi-solid material should exhibit high viscosity at rest, with a decrease in viscosity and a certain degree of fluidity under shear (for example, after passing through a tiny nozzle). Additionally, the material should quickly recover its viscosity after shear to prevent further flow after deposition onto the platform, maintaining the form.

Secondly, the diameter of the extruded filament should match the size of the nozzle. If the viscous component of the filament predominates (shear thinning) while passing through the nozzle, the viscosity of the extruded filament may increase, leading to shrinkage and, thus, improper dosage.

Thirdly, the filaments should possess self-supporting properties when printed in multiple layers. They should behave like a solid that resists deformation under gravity.

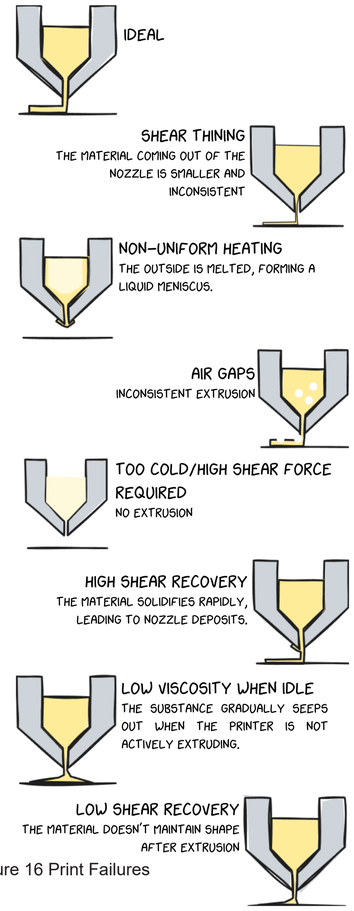


Figure 16 Print Failures

The process hinges on the material being malleable and yet structured. Overheating can turn it into a liquid, compromising structural stability, while insufficient heating renders it too rigid to extrude through the nozzle.

Most critically, non-uniform heating can cause parts of the formulation to liquefy, potentially causing settling. When settling occurs, the formulation becomes non-uniform, compromising the dosage accuracy. The formulation must be completely liquefied, mixed, and solidified to regain uniformity.

Most materials exhibit specific properties suitable for SSE within a narrow temperature range.

For example, Gelucire an common excipient is suitable for printing within a tiny temperature window (Fig. 17). Therefore, precise and uniform heating is crucial for accurate dosing with SSE tablets.

Despite the aforementioned complications, semi-solid extrusion (SSE) remains a prominent method for 3D compounding due to its distinct advantages over alternative

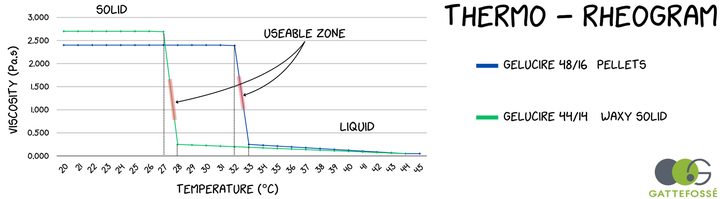


Figure 17 Thermo-Rheogram

techniques. SSE formulations enable higher drug loading, allowing the production of tablets with higher drug concentrations, which results in smaller tablet sizes. These smaller tablets are particularly beneficial for paediatric use, as they are easier for children to ingest. Additionally, tablets produced via SSE are more stable and uniform than suspensions, providing consistent compliant dosages.

Most SSE formulations can be printed at room temperature or at temperatures below 100°C, making the process both energy-efficient and compatible with a wide range of pharmaceuticals. The SSE setup is also relatively simple and inexpensive compared to other 3D printing methods.

SSE technology shows significant promise mainly in paediatric and oncological pharmaceuticals, especially for creating complex, multi-compartment, and personalised oral tablets. This method facilitates the production of tablets containing multiple drugs (poly-pharmacy) at a lower cost than other techniques. Furthermore, tablets produced through SSE require minimal to no post-processing, reducing time.

Beyond tablets, SSE is being explored for other oral preparations such as tapering medicines, demonstrating its versatility and potential in various clinical applications.

Key Takeaways

1. Although commercial tablet making is perfected, compounding is still relevant for sensitive populations.
2. The manual compounding process is cumbersome and requires much manual labour.
3. 3D compounding, although slower, can achieve perfect results consistently and is appealing

2.10 Previous on Concept Development

Refer to Confidential Appendix

Page Intentionally Left Blank

2.11 The Doser Rx1

2.11.1 Introduction

The Rx1 is Doser's offering in the 3D compounding space. The printer (Fig. 18) is a plug and play device reducing labour and time. Doser Rx1 aims to enable researchers to explore new drug formulations in multiple research fields such as: Systems Medicine, Tapering Medication, Combination Therapy and Modified release products. Shape, taste and colour can all be adjusted to achieve optimal treatment solutions. (Doser, 2024)

In its elemental state, every semi-solid 3D printer is an X,Y and Z gantry with an extruder.

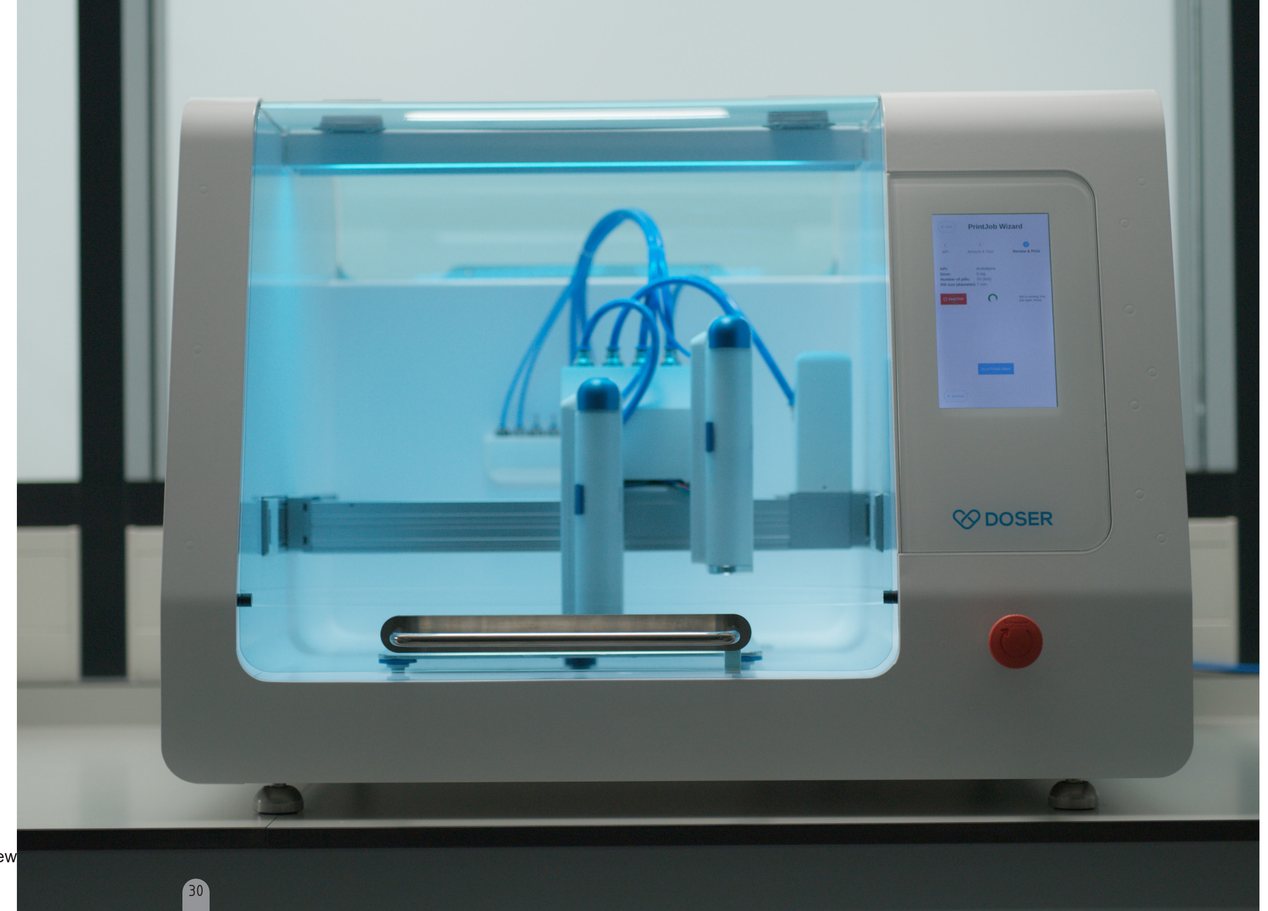


Figure 18 RX1 Front View

Doser has further developed this gantry system to make it useful for pharmaceutical 3D printing by making it complaint to the regulations and addressing the needs of the users. (Section 2.4)

2.11.2 Refillable Cartridges

Doser offers two sizes of cartridges a 5ml for smaller batches of tablets and a 40ml for larger batches of tablets. The recommended tablets weight for 5ml is between 25mg and 200mg, although larger sizes are possible but requires decreases the number of tablets printed. While the bigger 40ml cartridge can go up to 1200mg. The cartridges are made from stainless steel SEA316L.

2.11.3 Print Heads

The different print heads were developed to accommodate the different cartridges. The ESS (Extruder Small Screw) print head is for the smaller cartridge, while the EPM (Extruder Pneumatic Medium) for the bigger 40ml cartridge. (Refer Confidential Appendix)

As the name suggests, the ESS pushes the plunger using a stepper motor while the EPM uses an external air compressor to push the plunger. The compressor for the EPM print head is an external component.

The printer supports having multiple printheads on the gantry.

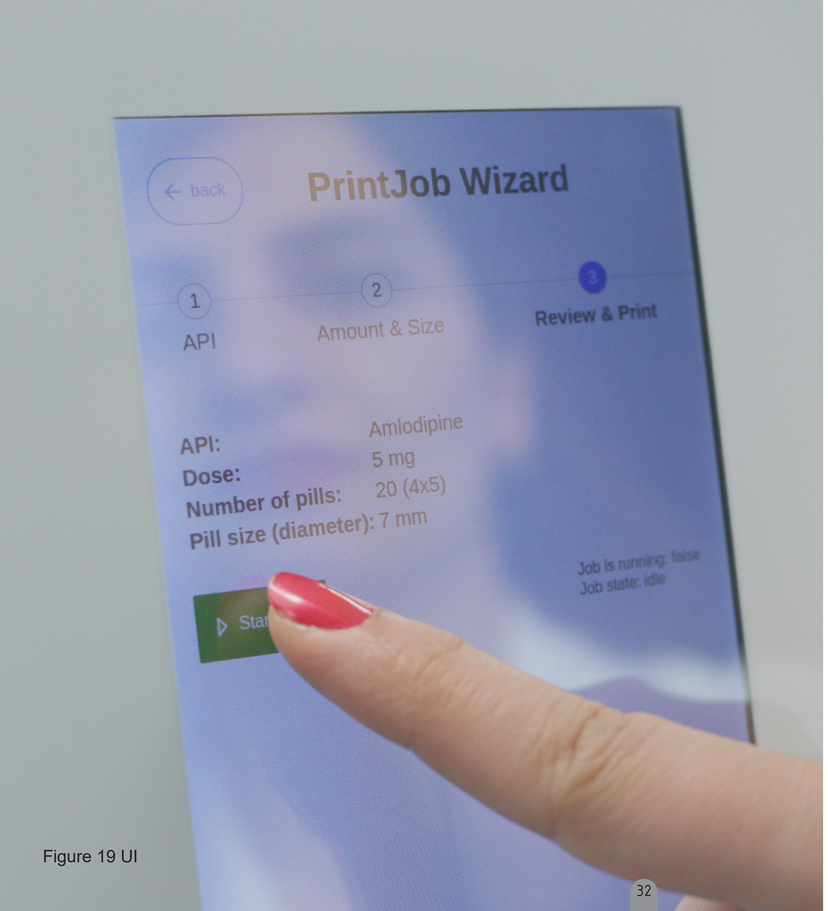


Figure 19 UI

2.12 Doser Rx1 Parts

The is a complex machine, looking at the bill of materials, it is made up of 327 parts with 227 unique components. A simplified block diagram of the printer is shown in the confidential appendix.

The three important parts according to me are the Print Heads, the XY gantry (right) and the control unit (left)

2.13 Working Principle

(Refer Confidential Appendix)

Figure 20 Gantry

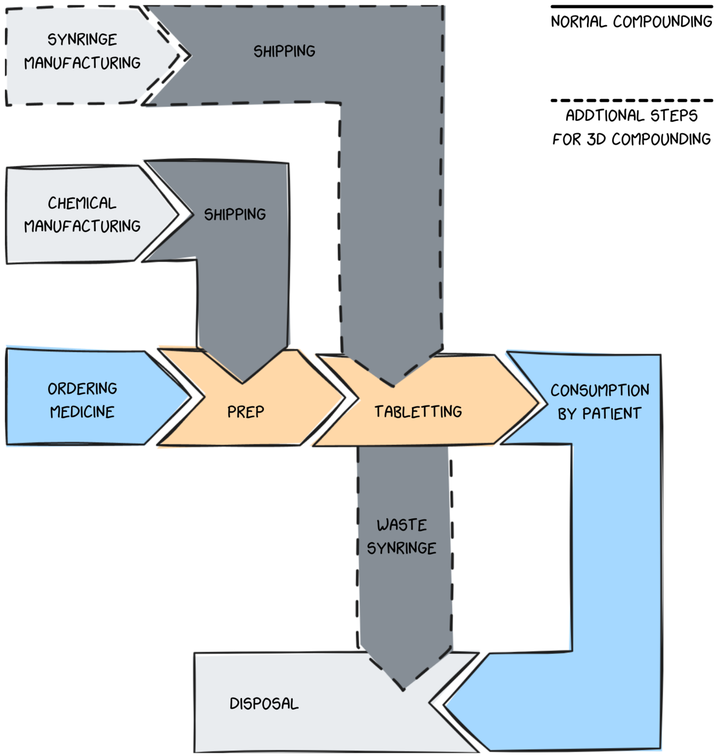


Figure 21 Supply Chain

2.14 Compounding Supply Chain

The current supply chain for personalised medicines follows a linear model. Figure 21 illustrates a simplified version of this system.

By examining the supply chain in this manner, I can:

1. Identify potential bottlenecks in production and distribution (out of scope)
2. Assess the environmental impact of different stages in the process (out of scope)
3. Evaluate opportunities for cost reduction and efficiency improvements
4. Anticipate regulatory challenges that may arise at various points in the chain
5. Explore possibilities for further innovation in personalised medicine delivery

This analysis emphasises the importance of considering not just the product but the entire ecosystem in which it is produced and delivered.

2.15 Doser Rx1 Intended Compounding Process

Doser's system consists of three main components: the printer, refillable cartridges, and medical formulations. The printer, located in pharmacies, prints tablets using cartridges filled with formulations. These cartridges can either be purchased pre-filled via a supplier or filled by the pharmacies on their own.

Upon deciding what to print, the pharmacist loads the filled cartridge into the printer, and sets the printing requirements.

The printing requirements, such as tablet count, tablet size, shape, and weight can be adjusted using PC software.

Depending upon the formulations, the additional parameters such has the cartridge heating temperature, time, extrusion rate also need to be tuned.

Currently, pharmacists manually adjust these settings, but in the future, pre-tested formulations will come with predefined parameters.

After use, cartridges need to be washed can send them back to the suppliers.

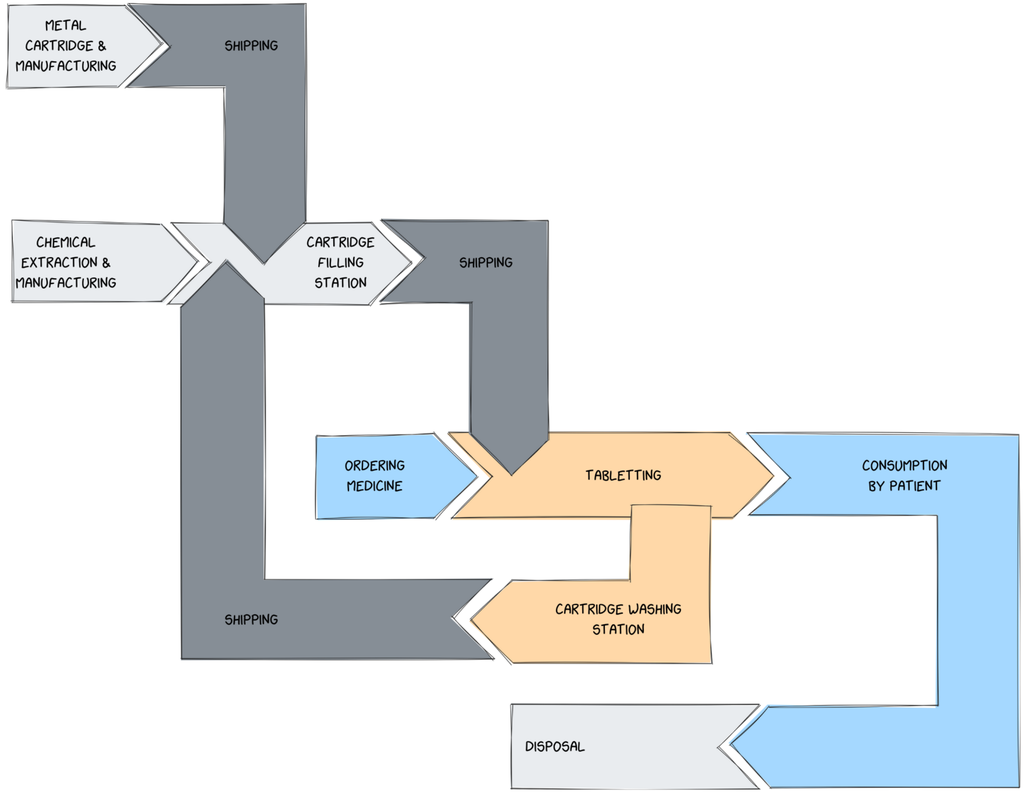


Figure 22 Doser's Intended Supply Chain

2.16 Doser Rx1 Product-System Architecture

Based on the working principles and intended process, I developed a system architecture to explore all potential relationships within the product. This provides a high-level overview of the product's architecture and how it is designed to function. (Fig. 23)

I utilised this diagram, along with a stakeholder matrix and the intended processes, to select participants for my user research.

The information about the self cartridge filling was gained through the field studies. (Section 3)

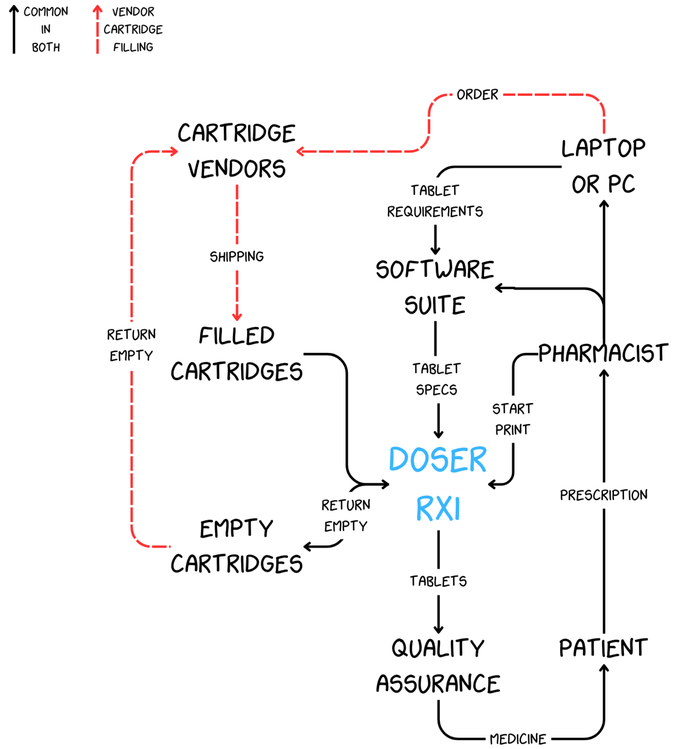


Figure 23 Architecture

3 Field Studies and Interviews

3.1 Introduction

The initial assignment in the graduation brief (appendix graduation brief) “Redevelop the Rx1 to enhance personalised drug manufacturing, catering to the needs of researchers and compounders in academic and pharmacy environments, improving efficiencies” indicates that the current compounding process using the Rx1 presents opportunities for improvement, particularly in terms of heating and cooling cycle times.

These prolonged cycles are causing production delays and potentially impacting end-user satisfaction. The lack of a standardised operating procedure across different user groups further complicates the situation. The stakeholder landscape for the Rx1 printer is diverse, encompassing at least two distinct user populations. Each group operates the printer in a different context, from large, clean rooms to standard desktop environments. This diversity in operational settings may contribute to the variation in printer performance and user expectations.

Furthermore, the Rx1 printer offers multiple cartridge sizes based on client needs. These cartridges have different physical properties due to volume and shape differences, likely impacting the heating and cooling cycles. The target printing temperature also varies based on the active ingredient in the cartridge, adding another layer of complexity to the process. To fully address the challenges and optimise the Rx1 printer’s performance and make it acceptable, it’s crucial to understand not only the technical aspects of the printing process but also the broader context of its use, including end-user requirements and the strategic vision of pharmacy owners.

3.2 Research Questions

RQ1: What are the use cases and contexts for the Rx1 printer’s use?

The Rx1 printer is employed in various settings, from commercial pharmacies to research facilities. Understanding these diverse contexts is crucial for optimising the printer’s performance. Commercial pharmacies may prioritise rapid production, while research pharmacies focus on formulation development. This question categorises and analyses the distinct operational environments, user expectations, and production goals across different Rx1 user groups.

RQ2: What are the critical variables in the Rx1 printing procedure?

The Rx1 printing process involves multiple variables (most of them unknown to me) affecting efficiency and output quality. These may include cartridge size, active ingredient properties, target printing temperatures, and environmental conditions. This research question seeks to identify and quantify the impact of each variable on the printing process, with a particular focus on how these factors influence heating and cooling cycle times. Understanding these critical variables is essential for developing a more standardised and efficient printing protocol.

RQ3: What are the specific end-user requirements for Rx1 across different operational contexts?

End-user requirements for the Rx1 printer vary significantly across different operational contexts. Commercial pharmacies may prioritise throughput and consistency, while research pharmacies might value flexibility and precision in formulation. This question aims to elucidate these diverse requirements and investigate how they relate to the printer’s heating and cooling cycle times. By understanding the relationship between user needs and technical constraints, we can identify potential areas for process optimisation or user expectation management.

3.3 Contexts and Study

In my stakeholder analysis, I identified following key spheres of influence: the end-users (patients), commercial pharmacies, and research laboratories.

End-Users: These are individuals who require personalised medication, such as paediatric patients or those with sensitive conditions like cancer.

I talked two guardians to understand their experiences with personalised medicine and whether they found it safer and more effective than standard pre-packaged medications.

Commercial Pharmacies: These pharmacies primarily handle prescriptions and supply medications, with less focus on research. I observed that staff, including lab technicians and compounders, approach the printer as a commercial product, expecting it to function seamlessly like any other commercial product.

They follow strict protocols and are uncertain how the Doser Rx1 will integrate into their existing workflows.

I conducted interviews with three individuals: a compounder, a lab technician, and the pharmacy owner, to grasp their expectations and how they envision the printer's role in their operations.

Research Labs: Located in universities and university hospitals, these labs focus more on research than on patient care. Staff here, often PhDs or postdocs, treat the printer as an experimental tool. They are open to exploring its capabilities, adjusting their processes, and providing feedback to Doser.

I spoke with two postdocs from different universities to understand their research goals and how the printer supports their work.

Doser's Internal Team: I also engaged with Doser's internal pharma team, which is responsible for testing and developing new formulations in collaboration with industry partners. This team provides quick feedback to the Doser design team and pushes the printer to expand its capabilities. Their role is crucial in refining the printer's performance and ensuring it meets both industry standards and user needs.

FIELD STUDIES OVERVIEW:

1 DOSER:

- INTERVIEWED CMC MANAGER, SENIOR PHARMACIST, AND INTERNS
- OBSERVED TABLET PRINTING, FORMULATION DEVELOPMENT, AND CLEANING PROCEDURES
- CONDUCTED NUMEROUS CASUAL INTERVIEWS AND OBSERVATIONS WHILE WORKING

2 COMMERCIAL PHARMACY:

- INTERVIEWED FOUNDER, PRINTER OPERATOR, AND COMPOUNDER.
- GAINED INSIGHTS INTO:
  - A) PHARMACY'S MISSION AND PRINTER EXPECTATIONS (FROM FOUNDER)
  - B) STAFF WORKING STYLES AND POTENTIAL PRINTER INTEGRATION
- THREE TOURS:
  - A) QA DEPARTMENT: UNDERSTANDING USER EXPECTATIONS
  - B) COMMERCIAL COMPOUNDING & CLEAN ROOM (TWICE): ANALYSING CURRENT PROCESSES FOR POTENTIAL PRINTER ADAPTATION

3 UNIVERSITY PHARMACY:

- INTERVIEWED TWO RESEARCHERS:
  - A) SPECIALIST IN PERSONALISED MEDICINES FOR PAEDIATRICS
  - B) SPECIALIST IN PERSONALISED MEDICINES FOR ONCOLOGY
- OBSERVED RESEARCHERS:
  - A) PRINTING TABLETS AND OPERATING MACHINERY
  - B) TRAINING A NEW INTERN ON MACHINE USAGE

Figure 24 Field Studies Overview

3.4 Observations

3.4.1 End-Users:

Patients in the Netherlands have a high degree of trust in their pharmacies.

Users often struggle with knowing how vigorously to shake liquid suspensions, which can affect the effectiveness of certain medications.

Although medicine bottles are usually filled with the exact required amount, administering medication to children often results in wastage. This can happen due to spilling, the child spitting it out, or even when parents take the medicine themselves to demonstrate its safety

Figure 25 Patient’s Medical Cabinet

perform multiple verifications. All calculations and measurements are done in the presence of the patient or parent, offering transparency and reassurance

Pharmacies are viewed as knowledgeable and caring, akin to an elder sibling who explains medications that patients may not fully understand and consults with doctors to ensure the patient’s best interests are prioritised.

This approach is particularly valued, as many patients do not fully comprehend their prescriptions, and doctors often do not explain the rationale behind their choices.

3.4.2 Compounding Pharmacies:

In the Netherlands, there are only 150 pharmacies authorised to produce their own medications, known as compounding pharmacies. All pharmacies in the country are prohibited from advertising their medications, so patients typically visit the nearest pharmacy first and may then be referred to a compounding pharmacy for more specialised treatment. In some cases, insurance companies also direct patients to specific pharmacies.

Compounding pharmacies can operate outside the constraints of patent laws when selling directly to patients. However, selling medications to other pharmacies requires different licences. While all the drugs they produce are listed in the national pharmacopoeia, each compounding pharmacy may make its own modifications, which are kept as trade secrets. These pharmacies have the flexibility to tailor medications to individual patient needs, such as altering excipients or adjusting dosages in consultation with the patient and doctor.

When asked about prefilled cartridges, compounding pharmacies are cautious. They prefer to use their own prepared medications, as these cartridges may be currently illegal, and there is concern that large pharmaceutical companies might lobby to restrict such practices. As a result, compounding pharmacies generally prefer to produce their own medications and fill cartridges independently, aiming for greater

Figure 26 Commercial Apotheek

control and vertical integration.

These small to medium-sized pharmacies are also investing in advanced technologies to stay competitive and appeal to patients. The smaller scale allows them to test and implement these innovations more quickly. In addition to using 3D printers, they are developing a robotic arm for inventory management and a 24-hour medicine vending machine.

Motivation for 3D printing:

A pilot programme is currently underway to assist patients in tapering off medications by creating personalised medicines. This service is being provided to 80 patients, all referred by insurance companies. As part of the pilot, the insurance companies collaborate with the

pharmacies.

The current tapering methods require patients to take varying amounts of tablets per dose, based on a chart, which relies heavily on patient compliance. This approach can lead to errors and difficulty in maintaining consistency. (refer appendix Tapering)v

Pharmacies view 3D printing as a solution to increase tapering compliance. They also agree it is the future of personalised medicine. would like to print 180 tablets per hour. They envision that the printer will be used multiple times a day during busy periods, and at least once a week otherwise.

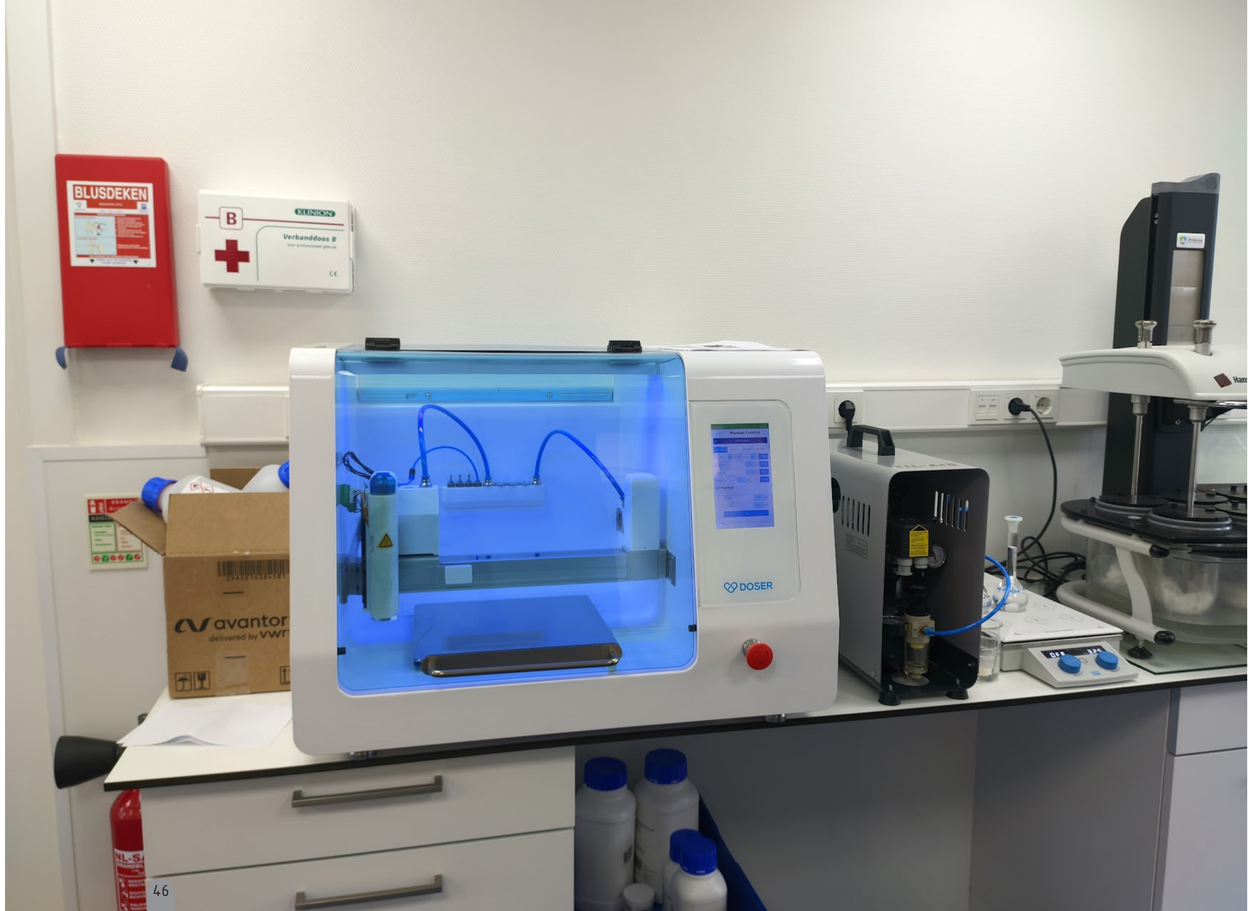


Figure 27 Commercial Apotheek - II

3.4.3 Commercial Compounders:

During my visit to the pharmacy, I observed that the machine was appropriately located in the Quality Assurance (QA) department, where it could be tested and validated to ensure all tablets meet regulatory standards. This setup is logical, given that the printer currently for research not commercial use.

During the pharmacy tour, I also saw other pharmaceutical machines used in compounding. It is standard practice for all pharmacists to keep a journal, typically in the form of a physical notebook. However, I noticed numerous sticky notes and random scribbles of information scattered throughout the area.

When I inquired about the current printer usage and associated issues, the major challenge identified was that the interface and interactions were overly complicated. The technician expressed doubt that others would be able to operate it effectively. They plan to move the machine to the clean rooms later once its validated.

When talking with a clean room employee, I got to know that the tasks in the pharmacy are generally linear. Each pharmacist is responsible for All equipment used must be thoroughly cleaned, dried, and in some cases disinfected, before use to prevent cross-contamination. This necessitates extensive planning to ensure that all necessary equipment is ready when tablets are to be made.

Figure 28 Commercial Apotheek - III

The pharmacist I spoke to follows a very linear process. Compounding is planned days in advance, and care is taken to ensure that all equipment, utensils, and machines required will be available. When they enter the clean room, they aim to complete all tasks before exiting, as re-entering is time-consuming and risks potential contamination.

To prevent contamination, the rules are strictly adhered to. However, repeated entry and exit from the clean room throughout the day increases the likelihood of errors, which the pharmacists also recognise. Therefore, they strive to minimise the number of times they enter and exit the clean room.

The actual tabletting is a relatively small part of the overall compounding process.

Compounding begins with receiving the prescription, mixing the formulation, and, in some cases, dehydrating or drying it. Extensive planning is required to ensure that everyone has the opportunity to prepare their medicines. Quality Assurance is conducted both physically (to ensure the tablets are correctly formed) and chemically (to verify the composition). Finally, the tablets are packaged in blisters or containers.

3.4.4 University Hospitals and Researchers:

The machine was kept in its own dedicated room within a clean room. The researchers also maintained a physical log of the machine in a journal, ensuring thorough documentation.

What surprised me was that in the commercial pharmacy, clean room practices and Good Manufacturing Practices (GMP) were only followed when compounding medicines. These medicines were not printed but were traditionally compounded for patients.

The researchers at the University Hospital, although currently only testing placebos, strictly followed all protocols. They had even developed their own Standard Operating Procedures (SOPs) for cleaning both the cartridges and the printer.

In contrast to the commercial pharmacists, the researchers mentioned that the printer's user interface was easy to use, and they reported no issues with it. However, during my visit, I observed the researchers train a new intern on the printer. There were many miss-clicks and errors, and the researcher frequently referred back to their notes. So, although they believe it to be user-friendly, it is clear that there is still room for improvement.

Compared to commercial pharmacies, the researchers' entire project revolves around the printer. Given the experimental nature of their work, they are accustomed to working

on multiple things in parallel or restarting from scratch when necessary. This approach contrasts sharply with that of commercial compounders. The researchers also have softer deadlines than commercial pharmacists; and are also okay with spending some extra hours in the evening to get a print done.

I found the researchers to be more curious about the machine; they acknowledged that it was a prototype and even suggested improvements that could enhance the system.

The researchers' compounding process was on a small scale. But also involved the same tasks weighing of ingredients, melting, mixing, solidifying, and then printing them. This was followed by weighing the tablets, purging the

Figure 29 Research Lab

cartridge, and cleaning both the cartridge and the printer.

The researchers utilized the printer for tasks beyond standard printing functions. For example, to purge any remaining formulation, they would increase the temperature and allow the material to flow out of the cartridge. Additionally, they cleaned the cartridges by filling them with isopropyl alcohol and purging them in the printer. They also stored the cartridges within the printer.

After filling a cartridge, they sometimes wiped it with cold water or held it under a tap to make it more comfortable to handle, reducing the temperature from 80°C to around 25°C.

3.4.5 Doser's Internal Pharma Team:

The pharmaceutical team at Doser comprises a CMC (chemistry, manufacturing, and controls) manager, a Senior Industrial Pharmacist, and a couple of interns. Doser operates from two locations: an engineering space and a pharmaceutical space. The pharmaceutical space includes a chemical lab where chemicals are stored, while the engineering space houses the printer. This arrangement allows the design team to provide support in case of malfunctions or failures. Towards the end of the thesis, the printer was relocated from the engineering space to the pharmaceutical space.

In terms of activities, the formulation preparation and cartridge filling occur in the pharmaceutical

space, whereas the printing takes place in the engineering space.

The Standard Operating Procedures (SOPs) developed by the internal team continuously evolve, occasionally leading to inconsistent adherence to the instructions during tablet printing. Like the university researchers, this team kept a journal and a log of the printer's activities. Notably, this team printed multiple formulations but did not have a formal identification method. Instead, they used masking tape to label the cartridges and applied it to the printer when a cartridge was used.

Additionally, the team was using an older version of the print head, which led to several

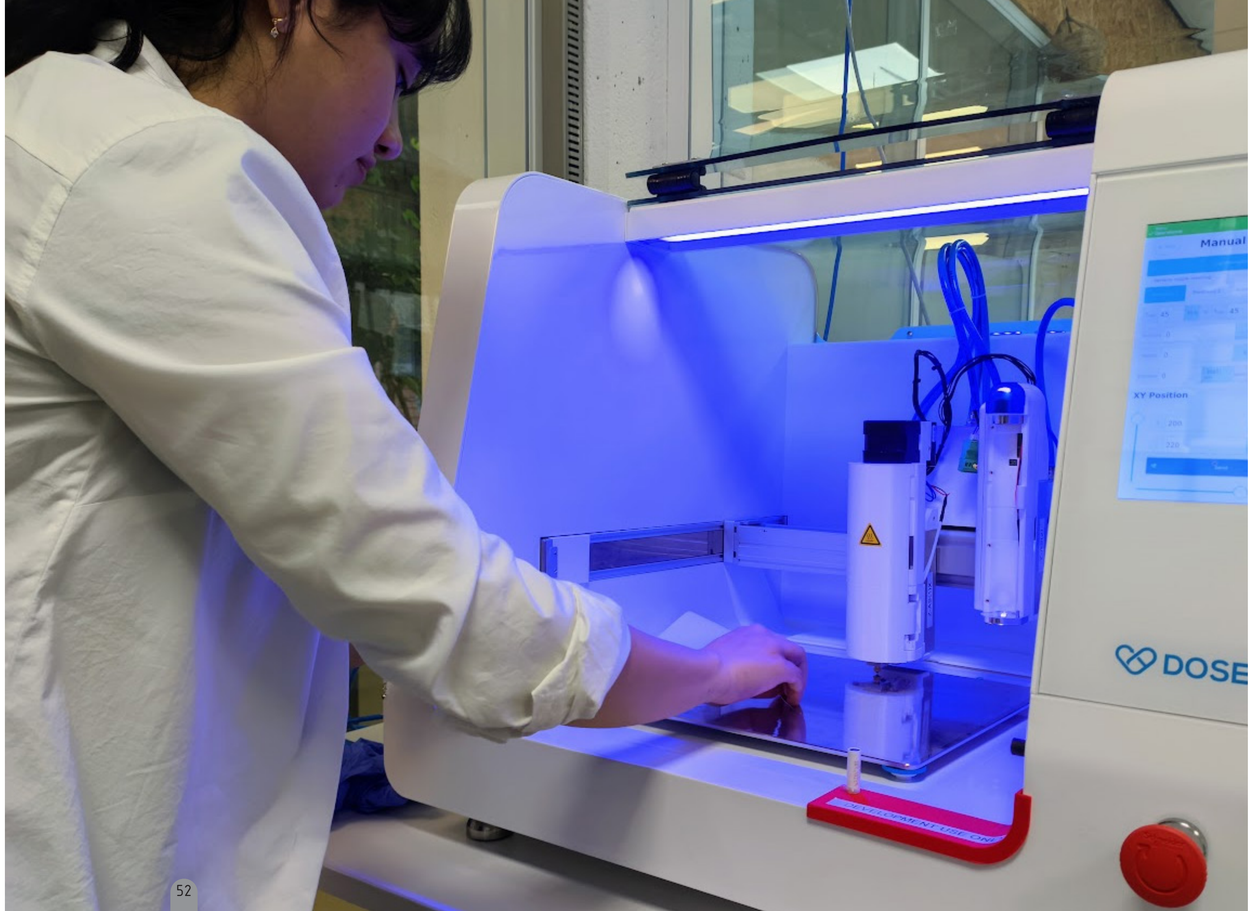


Figure 30 Doser's Space

unsuccessful attempts to preheat the cartridge. The compounding process was quite complex and involved multiple steps, similar to the procedures followed at a university hospita

3.4.6 My Personal Experience:

My experience with the printer was mixed. The printing itself was quite mesmerising, and the first time I printed ten tablets, I followed the intended process (see Figure X). During this time, the printing was straightforward, as I simply had to load the cartridge into the printer, preheat it for a certain period, and then begin printing. However, there was no feedback or indication of the remaining time remaining. I was impatient too waiting for the cartridge to preheat and attempted to prime it prematurely. This didn't work out as the material hadn't yet reached a semi-solid state.

After waiting a some more, we proceeded with bed levelling. My first attempt at bed levelling was unsuccessful as I struggled to get the right feel for the filler gauge and the distance between the nozzle and the bed. This caused the formulation to stick to the nozzle, resulting in inconsistent prints. Since these tablets were unusable, I had to restart the entire process, which took up additional time.

In another print attempt, I managed the whole process—from mixing the formulations to printing the tablets and then cleaning up everything. The entire process felt tedious, with many tasks that I believe could be automated.

Figure 31 Me working with the printer

3.5 Insights:

Regulatory

- Laboratories operate under varying regulations, leading to inconsistencies in compliance levels that often rely on individual discretion.
- Standard Operating Procedures (SOPs) for the printer are still being developed.
- Not everyone working in a compounding pharmacy has a pharmaceutical background.
- The responsibility for defining, implementing, and verifying protocols lies with pharmacists, while the compounding is carried out by others, which may result in variability in practice.

Ergonomic

- The printer is positioned at different heights across various locations, resulting in inconsistent ergonomic conditions.
- Minor cognitive slips can lead to significant setbacks, often requiring the entire process to be restarted.
- Commercial pharmacies operate on tight schedules, where failures or delays can increase cognitive stress.
- The work often demands that individuals remain on their feet for extended periods.
- The manual bed leveling procedure requires awkward postures, contributing to physical strain.

Operational

- A successful compounding process involves several key steps, but there are currently no dedicated tools to support these tasks, leaving the printer to handle some of them.
- For pharmacists, compounding includes preparing formulations, making or printing tablets, and cleaning up afterwards.
- In traditional compounding, various tools assist with these tasks. However, with the Rx1, there is no equipment available to mix, heat, purge, or clean the cartridges during 3D compounding, leading users to repurpose the printer for tasks it wasn't designed to perform.
- As the technology is still in its early stages, prefilled cartridges are not yet used, necessitating the development of a new process for operating the printer (Fig 34 and 35). This adds new tasks for the pharmacists and creates a new product-system architecture (Fig 32)
- This process also highlights another issue: there is often significant waiting time with insufficient actual printing.
- Most tasks are performed based on instinct or experience, introducing variability between users.

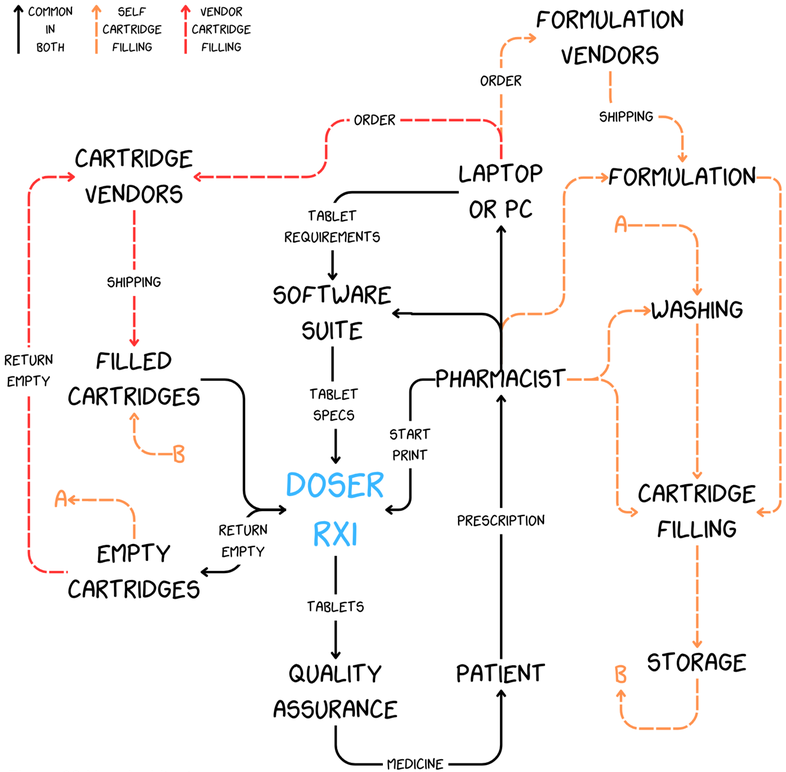
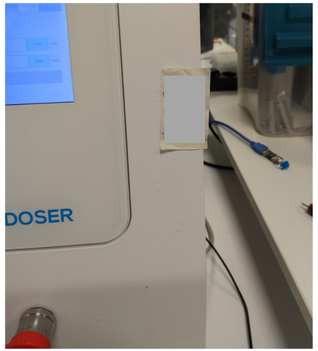


Figure 32 New Architecture

BED LEVELLING 'FEEL'

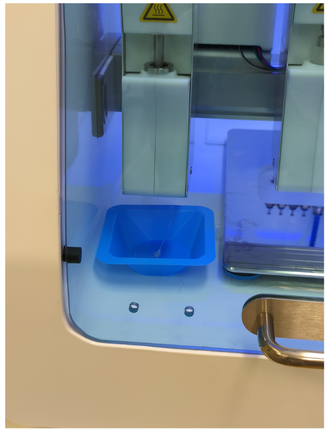
WHATS PRINTING



CARTRIDGE INGREDIENTS

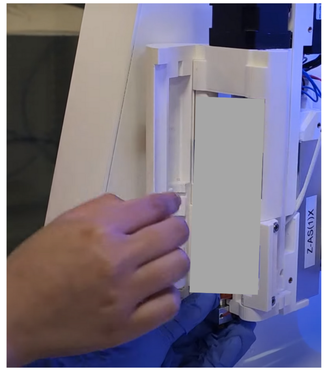
NEW INTERN TRAINING

PURGING THE CARTRIDGE (NON-INTENDED USE)

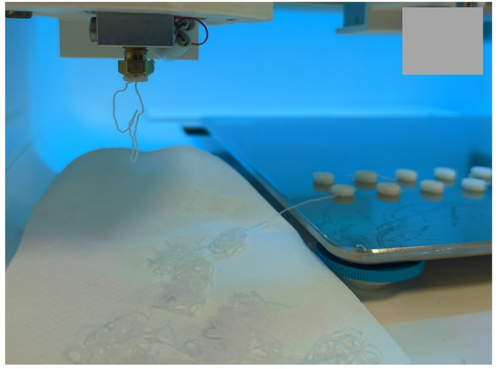


CAPSULE FILLING

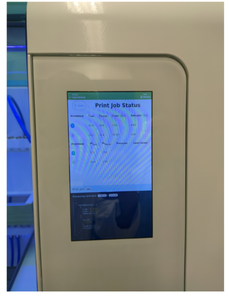
UI/UX PREFERENCES OF LAB TECHNICIANS



GLOVES FOR HAND IN CONTACT WITH API

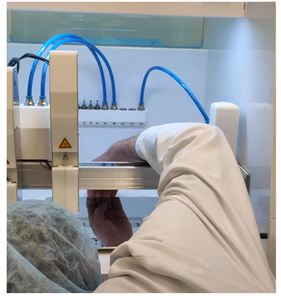


IMPOROPER BED LEVELLING



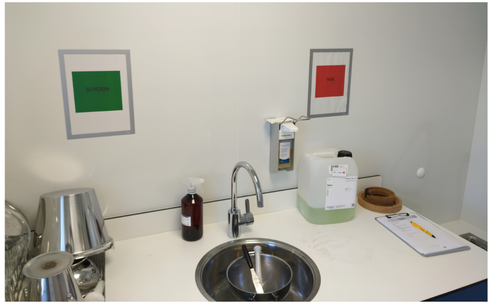
FEEDBACK IS LACKING

SANITASATION PROTOCOL



BED LEVELLING

TABLETTING MACHINE



GLP (GOOD LAB PRACTICES)
CLEAR AND COLOUR CODED SIGNS

Figure 33 Overview

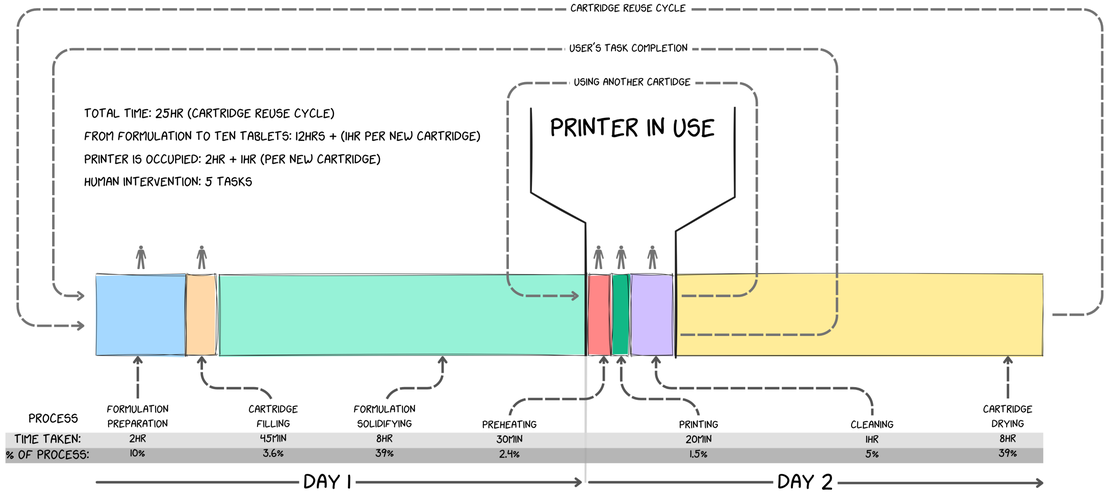


Figure 34 New Process

The new process illustrated in the figure above provides a clearer picture behind the users' frustrations. There is very little printing and a lot of prepping. It is seen that the actual use of the printer accounts for less than 10% of the total time, with the printing process itself taking only 1.5% .

A key insight from this process is that printing with the RX One typically takes two days. This extended timeframe is due to the need for formulations to solidify uniformly before printing can begin. Since there are no additional accessories or tools available, prefilled cartridges must be left to solidify for approximately 8 hours, usually overnight. Additionally, after a cartridge is emptied, it must be washed and thoroughly dried, as moisture can alter the properties of the formulation. Similar to the solidification process, cartridges are dried overnight.

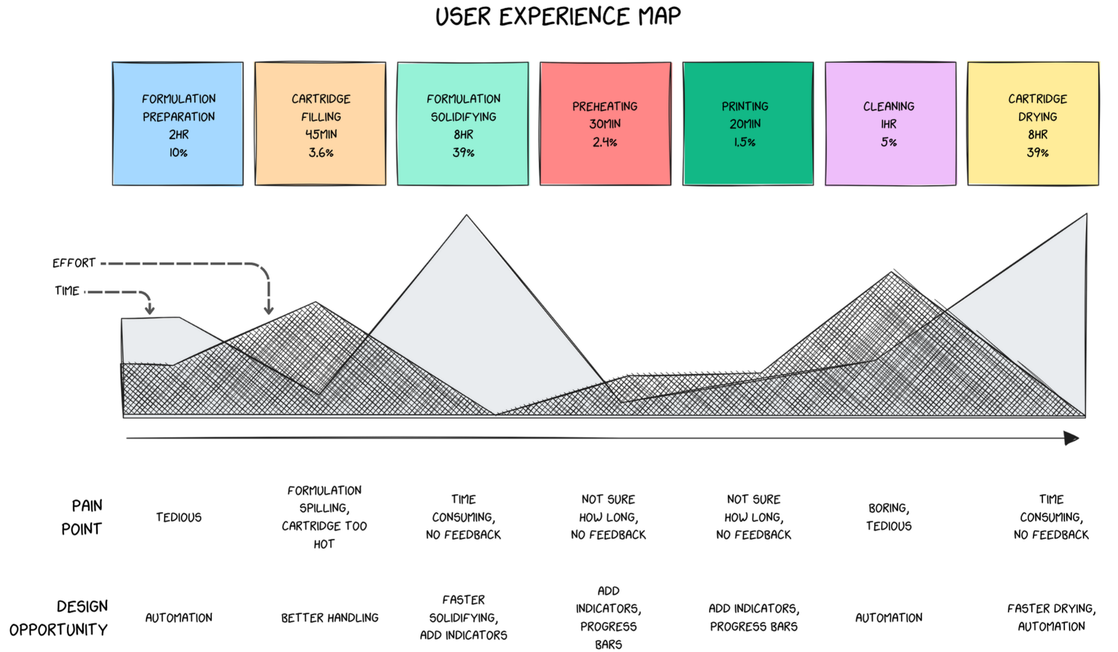


Figure 35 New Process - II

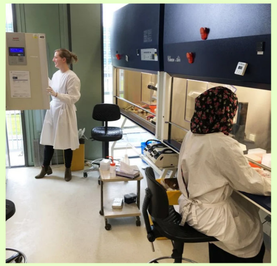
3.6 Personas

Based on the user research, I created three personas. These personas distill the key insights from our findings, representing the diverse needs, goals, and pain points of our target audience.

Each persona embodies a distinct user type, allowing us to tailor our design and development efforts to better meet the expectations and preferences of our users.

Furthermore, I gathered quotes from all user groups to capture authentic voices and direct feedback. These quotes provide valuable insights into the users' experiences and perspectives, adding depth and context to the

Figure 38 Persona

			CHALLENGES	MOTIVATION	DEMOGRAPHICS	GOALS
UNIVERSITY RESEARCHERS		DISCRETE WORKING HIGHLY FLEXIBLE HIGHLY METICULOUS HIGH PATIENCE	1. WORK-LIFE BALANCE. 2. UNFAVOURABLE RESULTS. 3. STAND ALL-DAY. 4. TIME CONSTRAINTS.	1. GETTING THE LUCRATIVE GRANT 2. FINISHING PHD	1. PREDOMINANTLY FEMALE 2. PHD OR A POSTDOC 3. AGE AROUND 30 4. IMPATIENT 5. EXPERIENCED IN PROTOCOLS 6. METICULOUS 7. FULL-TIME	1. PUBLISH PAPERS 2. PERFORM EXPERIMENTS AS PER PLAN 3. MINIMISE ENTRIES AND EXITS FROM THE CLEAN ROOM.
COMPOUNDER		CONTINUOUS WORKING HIGHLY RIGID HIGHLY METICULOUS LOW PATIENCE	1. MINIMAL WASTAGE 2. MAINTAINING GMP 3. MAINTAIN THE PRODUCTION RATE 4. WORK-LIFE BALANCE	1. EARNING MONEY 2. PROMOTIONS AND PROFESSIONAL GROWTH	1. PREDOMINANTLY MALE 2. AGE AROUND 25 3. IMPATIENT 4. USUALLY NOT FORMALLY EDUCATED IN THE FIELD 5. PART-TIME WORKER 6. FOLLOWS PROTOCOL SET BY SENIORS.	1. GET HOME QUICKLY. 2. MAKE NO MISTAKES. 3. COMPLETE DAILY TASKS.
COMMERCIAL PHARMACY		NOT APPLICABLE FLEXIBLE METICULOUS HIGH PATIENCE	1. BIG PHARMA 2. MAINTAINING GMP 3. STAYING RELEVANT 4. ATTRACTING CUSTOMERS	1. CREATING A LEGACY. 2. STAYING IN BUSINESS.	1. AROUND 50 EMPLOYEES 2. AVERAGE EMPLOYEE AGE 25 3. TRUSTED BY THE LOCAL COMMUNITY 4. CAN MODIFY MEDICINES TO SOME EXTENT 5. ONE OF FEW SMALL-SCALE DRUG MANUFACTURERS.	1. MAINTAIN PROFIT MARGINS 2. PROVIDE THE BEST CARE TO CUSTOMERS 3. STAY ON THE CUTTING EDGE 4. GROW WITH PARTNERSHIPS.

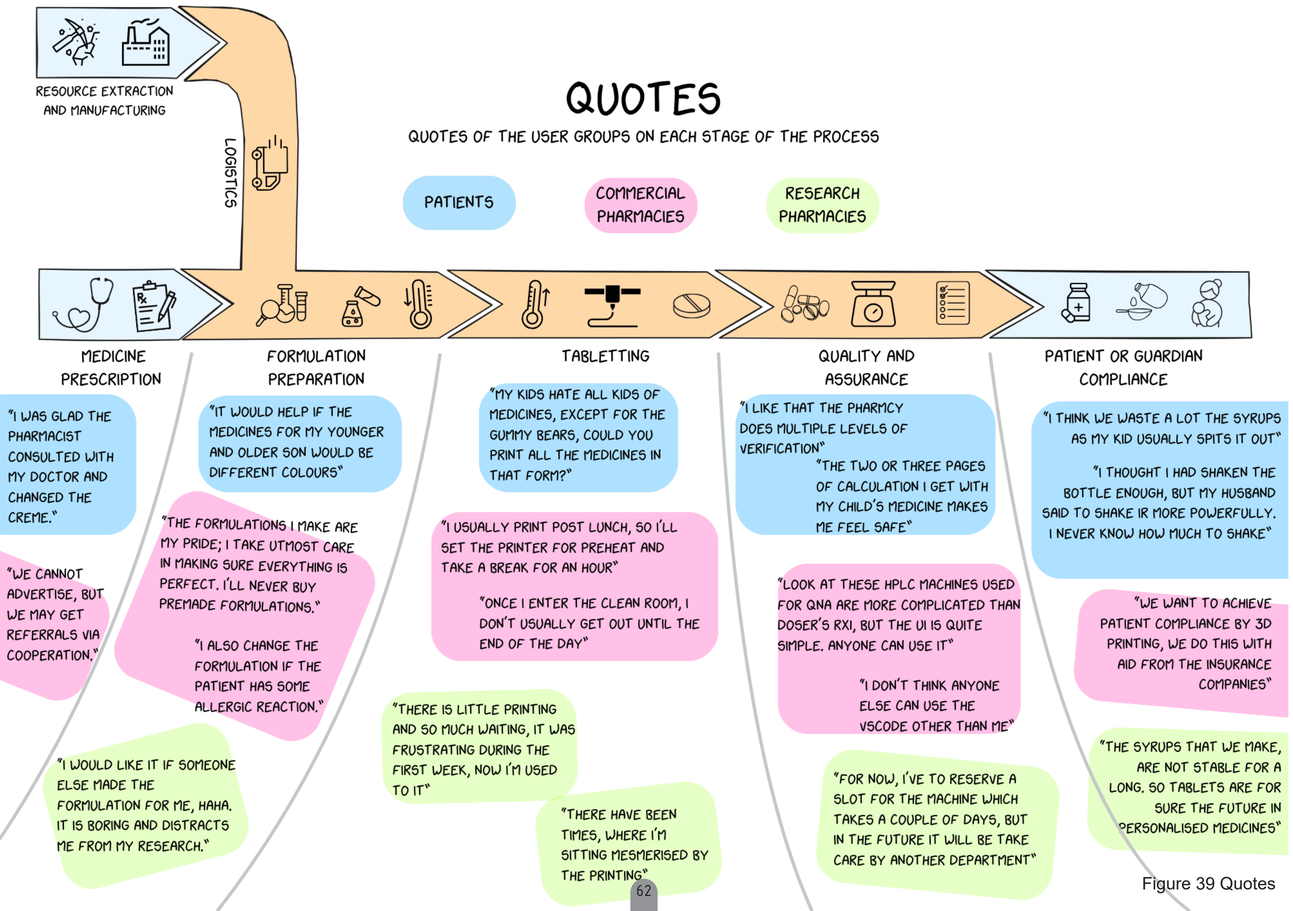


Figure 39 Quotes

personas. They help to ensure that our design decisions are grounded in real user sentiments.

Based on these quotes and the user studies, I created a persona for the company itself. This persona reflects how the company is perceived by users, offering a unique perspective on the company's image, strengths, and areas for improvement from the users' point of view.

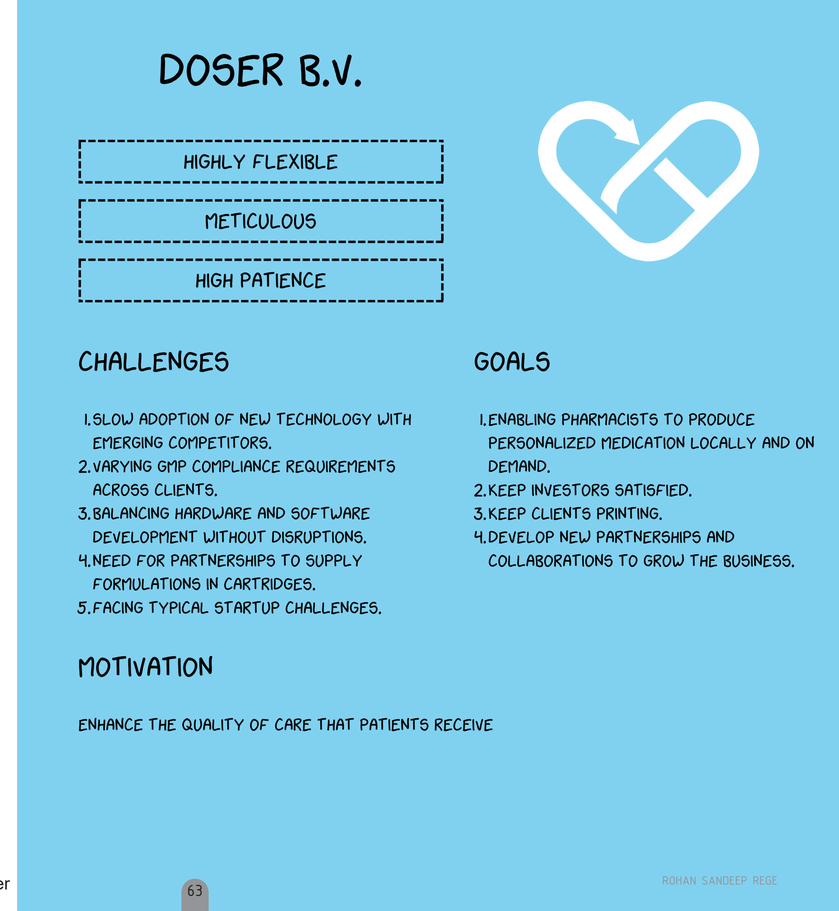


Figure 40 Persona - Doser

4 Design Requirements

4.1 Introduction

In this chapter, we integrate and synthesize the requirements identified in previous chapters. To enhance the robustness and relevance of our concept, we conduct three co-creation sessions with key stakeholders. These sessions serve as a bridge between my theoretical understanding and practical requirements.

4.2 Co-Creation (I) Problem Finding

Given the nature and complexity of the problem, I decided to utilize the Road Map for Creative Problem-Solving Techniques (Boom, 2019) , as well as techniques from Creative Facilitation (Tassoul, 2009).

I conducted a total of three creative sessions. The first two sessions focused on problem identification and solution exploration, while the third session concentrated solely on finding solutions. The process followed during these creative sessions is illustrated in Figure 41.

In the book, Boom outlines three key steps: problem finding, idea finding, and acceptance finding. I chose to implement the first two steps—problem finding and idea finding—in my approach.

For problem sensitisation, rather than following the recommended method of presenting the problem directly, I opted to use a fictional story to help participants empathize with the issue. Drawing from my observations at the commercial pharmacy, the university pharmacy and my personal experinces. I crafted a small fiction. Available in Appendix [FIX ME].

Using a story instead of a standard presentation to inform participants before a creative session increased engagement by capturing attention and sparked curiosity. The users also developed emotional connections through relatable characters and scenarios, and makes content more memorable.This approach reduced preconceptions, allowing participants to view problems from fresh perspectives.

Participants were asked to read the story, take notes, and then engage in a brief discussion to identify potential problems. Each participant was encouraged to choose one problem they considered most significant and explain their reasoning. This was followed by a rapid brainstorming session, where participants quickly shared any ideas that came to mind for solving the chosen problem. After the initial flow of ideas was exhausted, participants were given a break, and the session location was changed to reset their perspectives.

The second part of the session, which focused on solution finding, is detailed in Section 5.2. The problems identified during the first two sessions were then analyzed and refined. I integrated these findings with my own observations to define a new problem

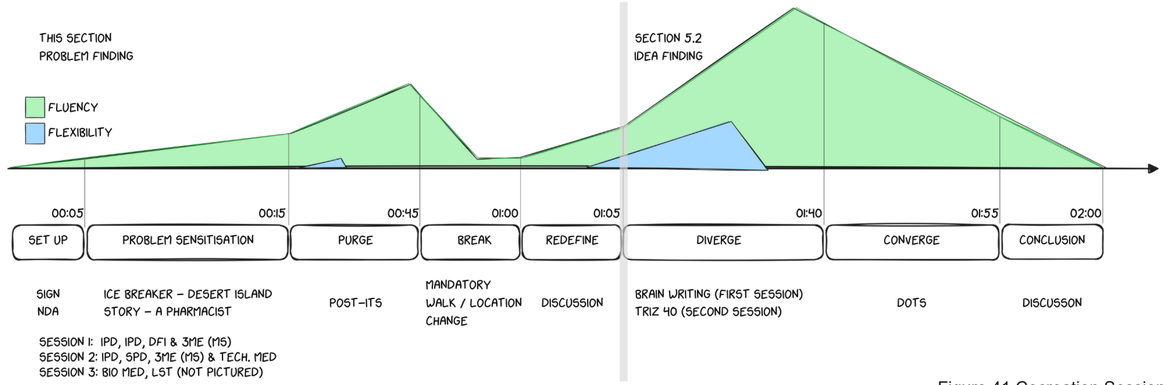


Figure 41 Cocreation Session

statement and set the goals for this thesis.

Identified Issues:

1. Repetitive and monotonous tasks
2. Extended waiting periods with no parallel tasks to engage in
3. Insufficient communication between lab technicians and the printer
4. Inconsistent results, with difficulty achieving perfection each time

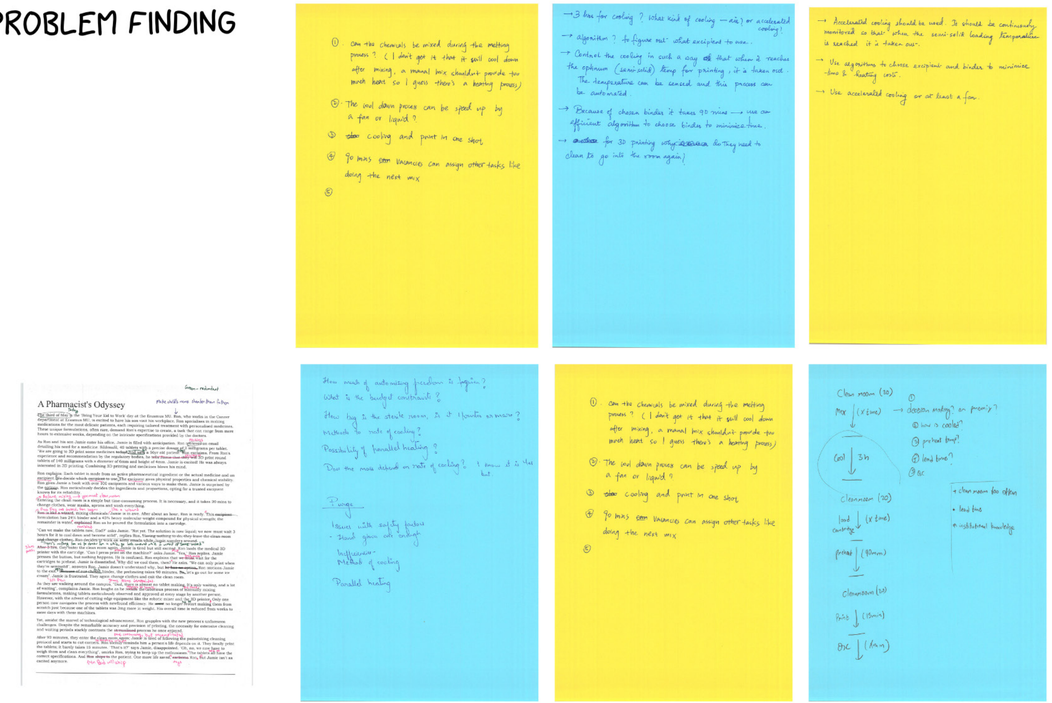


Figure 42 Problem Finding

4.3 List of requirements

I categorise the requirements and problems identified through my research into several distinct groups:

From Doser
These are requirements and issues raised by the individuals directly involved in dosing.

Indirect Stakeholders
This group includes stakeholders who are indirectly related to the printer but do not use it themselves, such as pharmacy owners, patients, and some post-doctoral researchers.

Direct Stakeholders:
These stakeholders are those who currently use or are expected to extensively use the printer in the future, primarily lab technicians, interns, and compounders.

Research:
This category includes insights gathered from the recent application discussed in previous chapters, as well as problems identified during the problem-finding phase of the creative sessions.

Each requirement is categorized accordingly, with a brief description of its design impact and linked to the previous chapters.

DOSER MEDICAL

CATEGORY	DESIGN REQUIREMENT	IMPLICATIONS ON DESIGN | SUB-REQUIREMENTS	REFERENCE
HEATING	THE PRINTER HEATS FORMULATIONS TO 90°C.	• THE DESIGN MUST WITHSTAND TEMPERATURES UP TO 90°C. • WARNING LABELS SHOULD BE PLACED WHERE NECESSARY TO INFORM USERS THAT CERTAIN PARTS MAY BE HOT. • ADDITIONAL SAFETY MAY BE REQUIRED IF THE USER NEEDS TO HANDLE THE CONCEPT WHILE IT IS HOT. • THE THERMAL PROPERTIES OF MATERIALS MUST BE ASSESSED BEFORE USE.	SECTION 2.2
CLEANING	THE PRINTER MUST BE CLEANED AFTER EVERY USE.	• EASY TO CLEAN, WITH ROUNDED EDGES AND AMPLE SPACE FOR HAND ACCESS. • RESISTANT TO CLEANING LIQUIDS LIKE ALCOHOL, SOAP, AND WATER, AND WITHSTANDS WIPING. • DIRT SHOULD BE EASILY NOTICEABLE, FOR EXAMPLE, BY USING A WHITE COLOUR.	SECTION 3.4
CLEAN ROOM COMPATIBILITY	THE PRINTER IS USED IN CLEAN ROOMS WITHIN PHARMACIES.	• MUST NOT ELECTROMAGNETICALLY INTERFERE WITH OTHER DEVICES. • COMPLY WITH WEEE AND CE GUIDELINES. • FUNCTION PROPERLY IN ENVIRONMENTS WITH TEMPERATURES BETWEEN 16°C AND 19°C AND RELATIVE HUMIDITY BETWEEN 55% AND 65% (CLEAN ROOM CLASS 7). • MATERIALS USED SHOULD BE RESISTANT TO SHEDDING.	SECTION 2.4 (REGULATIONS)
MATERIAL COMPATIBILITY	ONLY PHARMACEUTICALLY INERT MATERIALS MAY CONTACT MEDICAL FORMULATIONS.	• LIMITATIONS ON MATERIALS BEING USED. • LIMITATIONS ON THE MANUFACTURING PROCESSES. • POSSIBLE INCREASE IN COST.	SECTION 2.4 (REGULATIONS)
GMP AND GAMP	ALL DEVICES MUST ADHERE TO GMP AND AUTOMATED GMP STANDARDS.	• THE DESIGN SHOULD PROVIDE INDICATORS FOR ANY DEVIATIONS FROM THE STANDARD PROCESS. • THE DESIGN MUST BE AUDITABLE, WITH APPROPRIATE DOCUMENTATION AVAILABLE.	SECTION 2.4

INDIRECT STAKEHOLDERS

CATEGORY	DESIGN REQUIREMENT	IMPLICATIONS ON DESIGN | SUB-REQUIREMENTS	REFERENCE
PRODUCTIVITY	INCREASE THE PRODUCTIVITY OF THE PRINTER	• MAINTAIN OR REDUCE THE TABLET PRINTING SPEED. • THE CYCLE TIME OF THE PRINTER SHOULD BE THE SAME OR REDUCED. • NOT CAUSE ADDITIONAL DOWNTIME TO THE PRINTER.	SECTION 3.4
AUTONOMY	MAINTAIN AUTONOMY OF THE PHARMACIES	• ALLOW PHARMACIES TO FILL THEIR CARTRIDGES. • WORK WITH CARTRIDGES FILLED BY THE PHARMACIES AND THOSE BOUGHT FROM OTHER VENDORS.	SECTION 3.4
REGULATIONS	THE DESIGN SHOULD COMPLY WITH THE REGULATIONS OF THE PHARMACIES	• THE DESIGN SHOULD ADDRESS INDIVIDUAL GMP REGULATIONS PER LAB. • THE DESIGN SHOULD COMPLY WITH THE STRICTEST RULES.	SECTION 2.4
PATIENT	THE DESIGN SHOULD MAINTAIN OR IMPROVE THE CURRENT PATIENT–PHARMACY RELATION	• SHARING SUPPORTING DOCUMENTS, SUCH AS PREPARATION LOGS AND COMPLIANCE TEST RESULTS, SHOULD BE POSSIBLE WITH THE PATIENT. • ALL DOCUMENTS SHARED WITH THE PATIENTS MUST BE IN A NON-MEDICAL, EASILY READABLE FORMAT.	SECTION 3.4

DIRECT STAKEHOLDERS

CATEGORY	DESIGN REQUIREMENT	IMPLICATIONS ON DESIGN | SUB-REQUIREMENTS	REFERENCE
PRODUCTIVITY	THE DESIGN MUST NOT AFFECT THE PRODUCTIVITY OF THE LAB TECHNICIANS	• WORK AROUND THE FLEXIBLE NATURE OF RESEARCHERS. • FIT INTO THE LINEAR WORKING STYLE OF COMMERCIAL PHARMACIES. • MAINTAIN OR INCREASE THE RELIABILITY OF THE PRINTER.	SECTION 3.4
INTERACTION	MAINTAIN OR IMPROVE USER ACCESSIBILITY	• SUITABLE FOR MBO-LEVEL EDUCATION USERS. • INCORPORATE VISUAL CUES RATHER THAN TEXT. • PROVIDE USER FEEDBACK. • REFLECT USERS' AESTHETIC PREFERENCES.	SECTION 3.4

RESEARCH

CATEGORY	DESIGN REQUIREMENT	IMPLICATIONS ON DESIGN | SUB-REQUIREMENTS	REFERENCE
SPATIAL	THE DESIGN SHOULD MATCH THE SPATIAL CONSIDERATIONS IN THE PHARMACIES	• THE DESIGN SHOULD OCCUPY AN AREA OF 80X80CM, SIMILAR TO A TABLETOP • THE HEIGHT OF THE DESIGN SHOULD BE AROUND 40CM. • WORK WITH A STANDARD WALL OUTLET PROVIDING MAX 16A.	SECTION 3.4 OBSERVATIONS
PRINTER USE – CONGITIVE ERGONOMICS	THE DESIGN SHOULD REDUCE THE COGNITIVE TASKS FOR THE USER.	• INDICATE TO THE USER THE CURRENT STAGE OF THE CARTRIDGE IN THE PROCESS. • THE USERS SHOULD BE ABLE TO IDENTIFY THE FORMULATION PRESENT IN THE CARTRIDGE. • INDICATE THE AMOUNT OF FORMULATION LEFT IN THE CARTRIDGE.	SECTION 3.4 OBSERVATIONS
PRINTER USE – PHYSICAL ERGONOMICS	THE DESIGN SHOULD REDUCE THE PHYSICAL STRAIN ON THE USER.	• THE DESIGN SHOULD ENABLE ONE-HANDED USE • NOT CAUSE DISCOMFORT WHEN USED FROM A HEIGHT OF 80 CM. AVG. TABLE HEIGHT.	SECTION 3.4 OBSERVATIONS
PRINTER USE – ORGANISATIONAL	THE DESIGN SHOULD BE ABLE TO PLAN TASKS WITH THE USER	• PROVISIONS FOR THE USERS IN PREPLANNING AND PRINT JOB SCHEDULING. • ALLOW FOR REMOTE MANAGEMENT AND CONTROL.	SECTION 3.4 OBSERVATIONS
REGULATORY (FUTURE-PROOFING)	THE DESIGN SHOULD USE THE PRINCIPLES OF 'LONG-USE'	• ASSEMBLIES SHOULD BE EASILY SEPARABLE. • AVOID USING GLUE IN THE DESIGN. • USE MODULAR COMPONENTS. • ENSURE EASY DISASSEMBLY INTO SUBCOMPONENTS.	SECTION 3.4 OBSERVATIONS

Given the extensive scope of of the project and the time constraints of this thesis, it is not feasible to address and validate all the requirements within this timeline. However, it is essential to keep these considerations in mind to ensure that my design directions remain aligned with the overall objectives.

After consulting with the company, my academic advisors, and mentors, I have decided to focus on the following categories.

1. Heating
2. Productivity
3. Autonomy
4. Interaction
5. Printer use

Figure 43 Problem Finding - Session

5 Ideation

5.1 Introduction

The ideation process was an ongoing phase that commenced at the project's outset and persisted until I received the greenlight. Initially, my ideas centred primarily on the 'product', as I was unfamiliar with the process. Most of my concepts revolved around the initial problem statement provided by Doser. These early ideas gradually evolved as I conducted more user tests and gained insights.

In the first few months of the project. At this stage, I lacked a clear understanding of the problem statement and the challenges faced by pharmacists. With limited input from clients, the ideas generated were straightforward and incremental rather than groundbreaking. These early concepts focused on basic improvements to assist those working with the printer.

As I began conducting user interviews and personally 'playing' with the printer, my ideas matured. I started identifying latent problems experienced by the users. This stage also included creative sessions focused on problem-finding, allowing me to develop more refined concepts. I paid greater attention to the holistic process of using the printer rather than just developing a small part of it.

In the final stage, the ideas became more sophisticated and were deemed viable for further development. These concepts were a combination of insights from the creative sessions and my original ideas. At this point, the ideas were well-formed, incorporated a new process, and were ready for refinement and implementation.

A brief overview of the ideation can be seen in figure 44 on the next page.

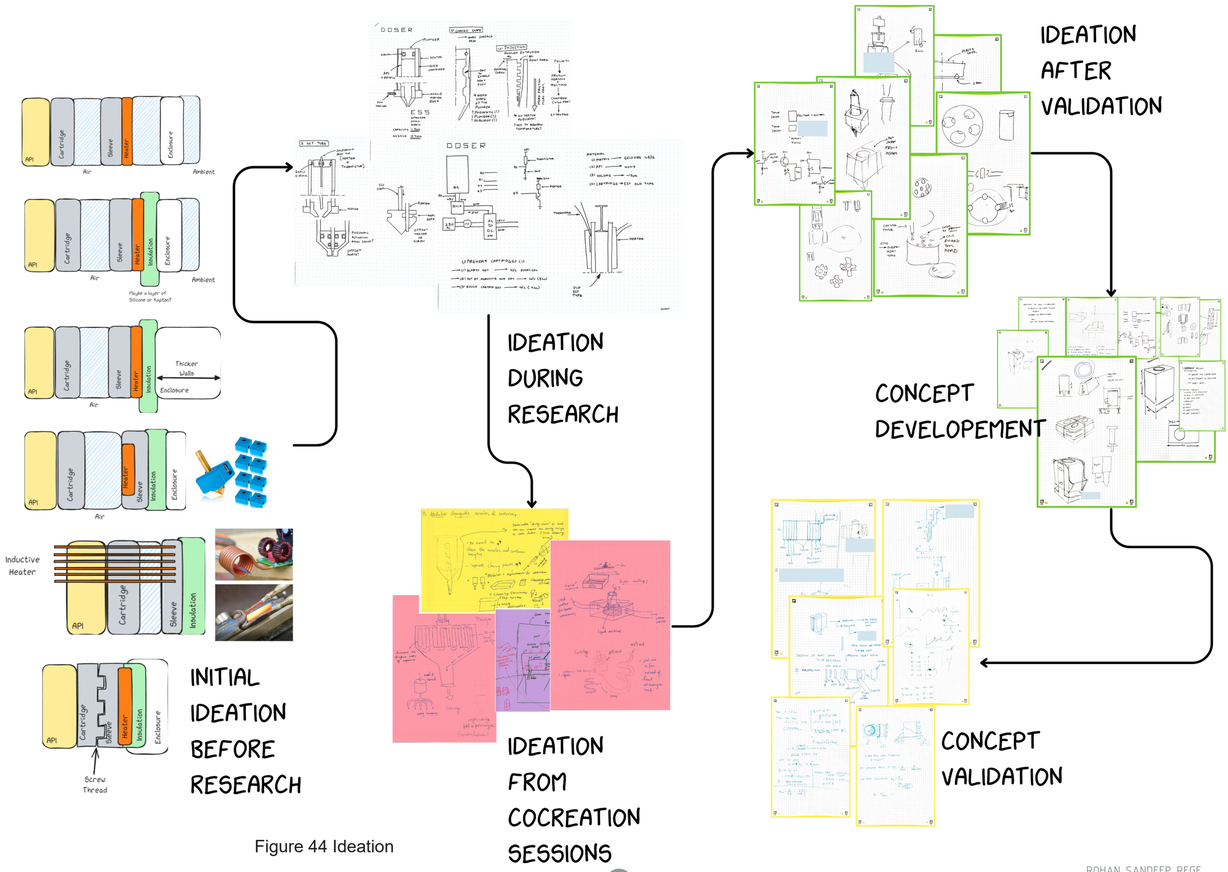


Figure 44 Ideation

5.2 Co-Creation (II) Solution Finding

I conducted three creative sessions in total. The first two sessions focused on identifying problems and exploring potential solutions, while the third session was dedicated solely to solution development. The process followed during these sessions is illustrated in Figure 42.

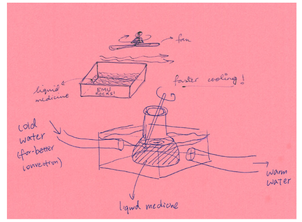
For the solution-finding phase, two methods were employed: TRIZ 40 and brain writing. Both methods were selected based on Creative Problem-Solving Techniques (Boom, 2019).

Brain writing was chosen for two reasons: it is particularly forgiving and easy for non-designers to quickly generate ideas, making it ideal for a novice facilitator like me.

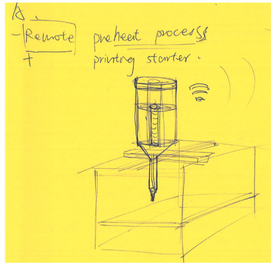
TRIZ 40, although somewhat complex to facilitate, was selected to aid in my professional growth and because it is recommended for addressing more engineering-oriented problems (Tassoul, 2009).

Since most of the participants were not industrial desingers, it proved challenging to conduct the sessions, as they preferred to write rather than sketch ideas.

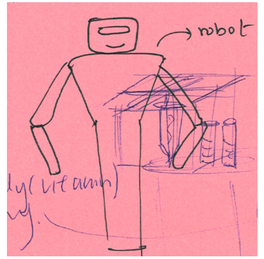
The chosen ideas are shown in Fig. 45



FORCED COOLING



REMOTE PREHEATING



AUTOMATED CLEANING & DRYING

Figure 45 Idea Finding

Page Intentionally Left Blank

6 Cartridge Plus Ecosystem

6.1 A new process

The new process is central to the design concept. As illustrated in Figure 46, the updated process reduces the time from formulation mixing to medicine production to 6 hours, a significant improvement over the previous method (Fig. 34, 35). The enhanced efficiency is further supported by the reduced need for drying, as medicines can now be reused.

Additionally, the Cartridge Plus, includes an integrated heater, accelerates the drying process for the cartridges.

Furthermore, the number of required human interventions has been decreased from five tasks to three.

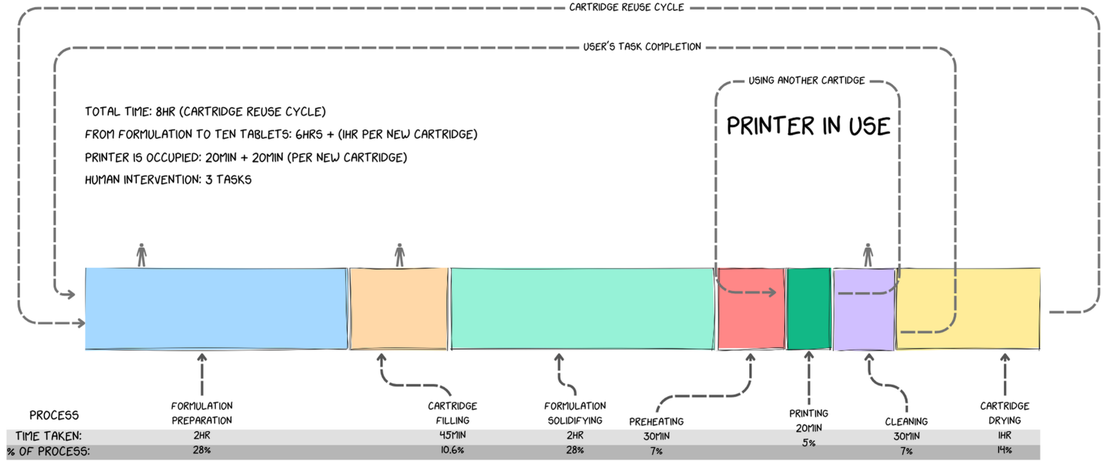


Figure 46 New Process

6.2 The Cartridge Plus

The Cartridge Plus is an advanced, smart cartridge designed to enhance the precision and functionality of the printing process. It features an integrated Peltier module that enables precise heating and cooling of the formulation, ensuring optimal conditions for formulation stability and print quality.

A key innovation of the Cartridge Plus is its onboard memory module, which stores detailed information about the formulation, including material composition, temperature settings, and environmental conditions. This memory allows the cartridge to communicate directly with the printer, facilitating real-time adjustments and improving the accuracy of the printing process.

To ensure user safety and comfort, the Cartridge Plus includes small insulated dips on its sides. These insulation features protect the pharmacist from the heat generated by the cartridge, reducing the risk of burns during handling. The dips are removable and can be replaced with differently colored inserts. These color-coded inserts aid in identifying and grouping various cartridges, enhancing organization and efficiency.

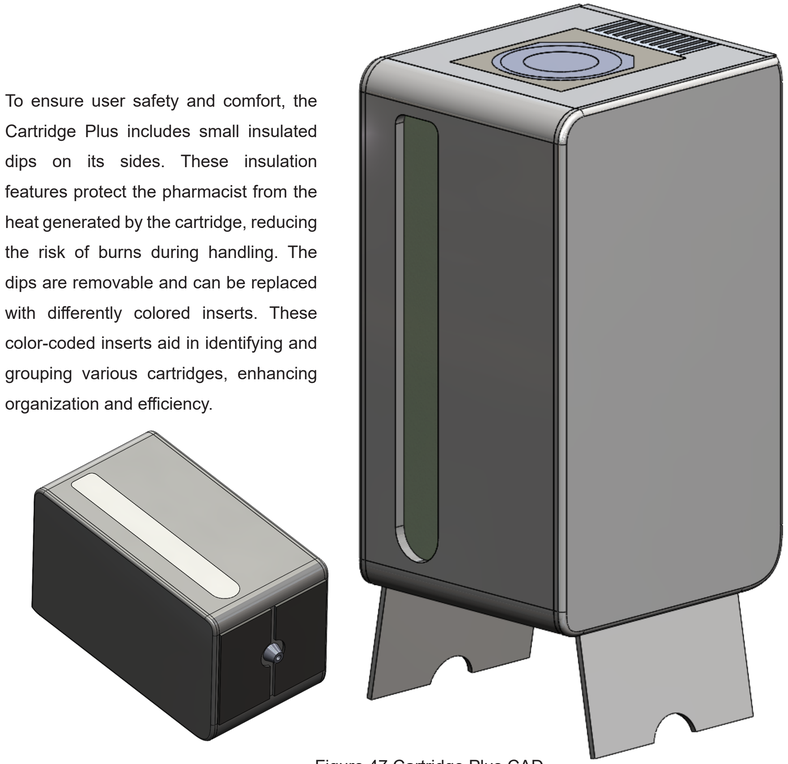
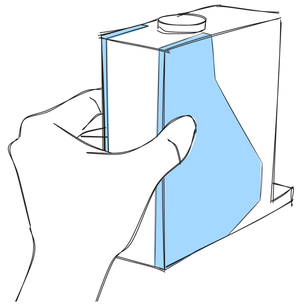


Figure 47 Cartridge Plus CAD

Additionally, the Cartridge Plus is equipped with a small LED indicator that provides crucial information about the cartridge's status. The LED displays the amount of formulation present and indicates the stage of the formulation, such as whether it is in a semi-solid state, ready for printing, or undergoing cooling or preheating. These indicators are particularly useful for distinguishing cartridges during storage and ensuring that the correct formulation is used at the appropriate time.

The design also includes small retractable flaps



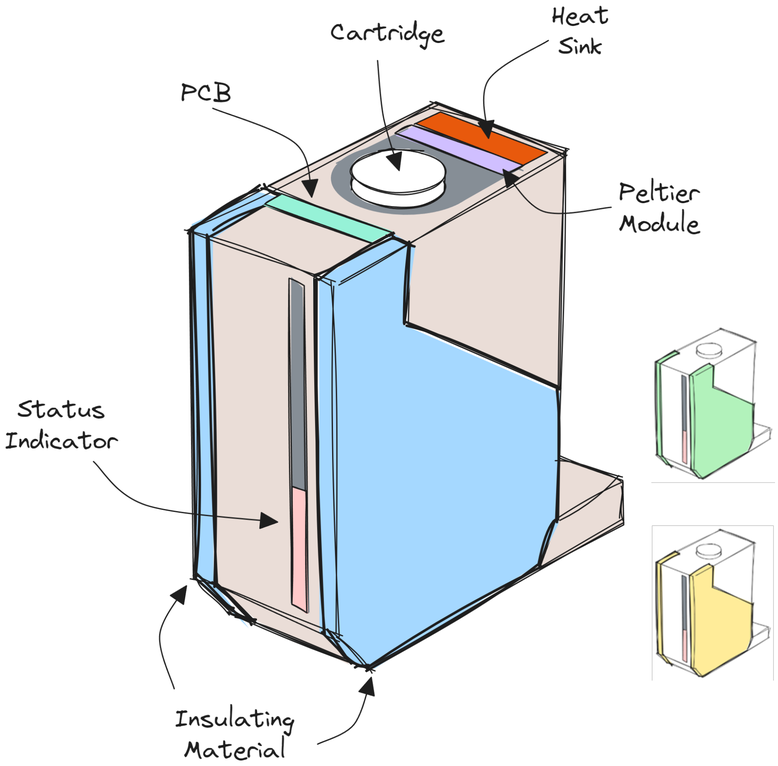
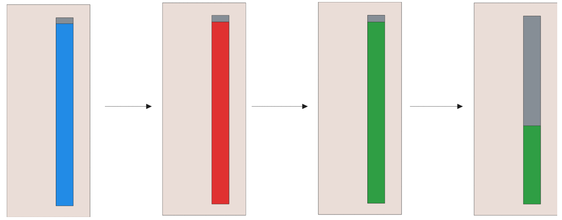
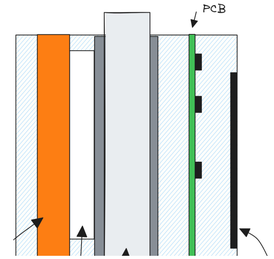


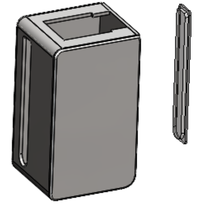
Figure 48 Cartridge Plus

at the bottom of the cartridge, which serve a temporary purpose during storage or handling. When the cartridge is inserted into the printer's print head, these flaps automatically fold flat, ensuring they do not obstruct the printing process.

Overall, the Cartridge Plus integrates several advanced features to optimize the printing process, enhance usability, and improve safety, making it a crucial component of the modern printing system.







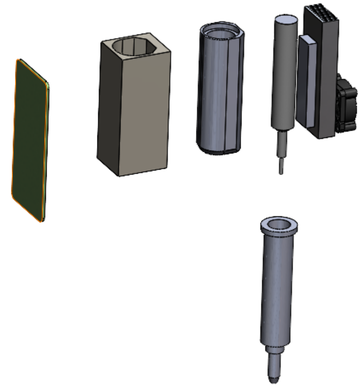


Figure 49 Cartridge Plus - Crossection

6.2 The New Printhead

The Cartridge Plus integrates seamlessly with an updated print head design, which, while similar to its predecessor, introduces significant enhancements in functionality. The primary difference lies in the relocation of the heating and cooling elements. In the previous design, these elements were housed within the print head. However, in the new system, they have been moved to the Cartridge Plus, allowing for better thermal management.

When the Cartridge Plus is connected to the print head, the connection is secured by magnets (not pictured) and holes to ensure a stable and accurate attachment. Unlike the older print head, the new design leverages the smart capabilities of the Cartridge Plus, which stores detailed information about the formulation, including its composition and current state (e.g., temperature, semi-solid status). The print head reads this information and automatically adjusts its operational settings and profiles to match the specific requirements of the material being printed.

As the printer operates, it tracks the position of the plunger within the cartridge, continuously updating the display to show the remaining amount of material. This information is also transmitted to the remote management software, providing users with a real-time overview of cartridge status across multiple devices. This feature ensures that pharmacists and researchers are always aware of material levels, facilitating better planning and inventory management.

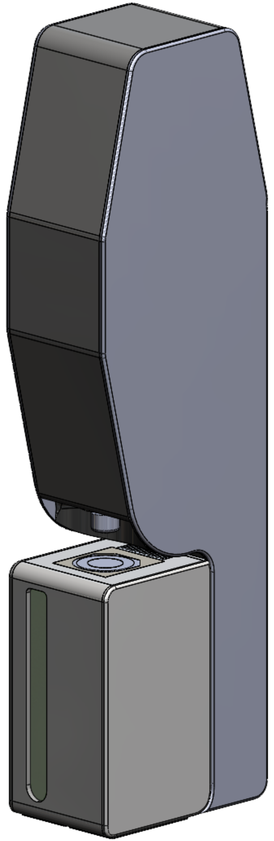


Figure 50 New Printhead

Furthermore, through the print head, the printer can set custom profiles for each cartridge, optimising the printing process for different formulations. This level of customisation enhances the printer's versatility, allowing it to handle a wide range of pharmaceutical products with precision and consistency.

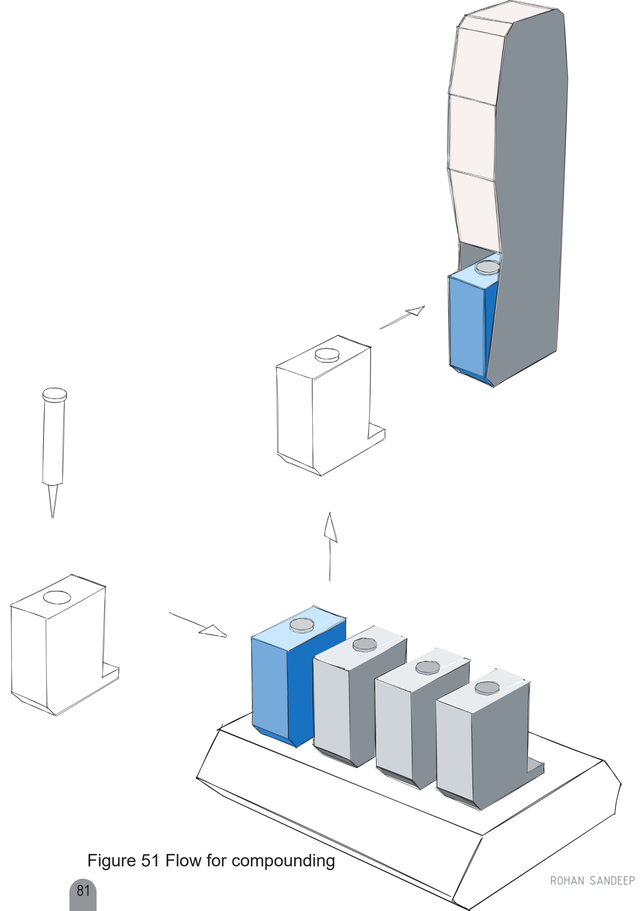


Figure 51 Flow for compounding

6.2 The Base Station

The Base Station serves as the third essential component of the Cartridge Plus ecosystem, complementing the functions of both the Cartridge Plus and the print head. Much like the print head, the Base Station is designed to interface directly with the Cartridge Plus, providing comprehensive control over its functions. However, unlike the print head, the Base Station does not include an extruder, as its primary purpose is not to print the formulation but to manage and prepare the cartridge for future printing tasks.

Once a cartridge is filled with the desired formulation, it can be placed on the Base Station for various configurations and pre-

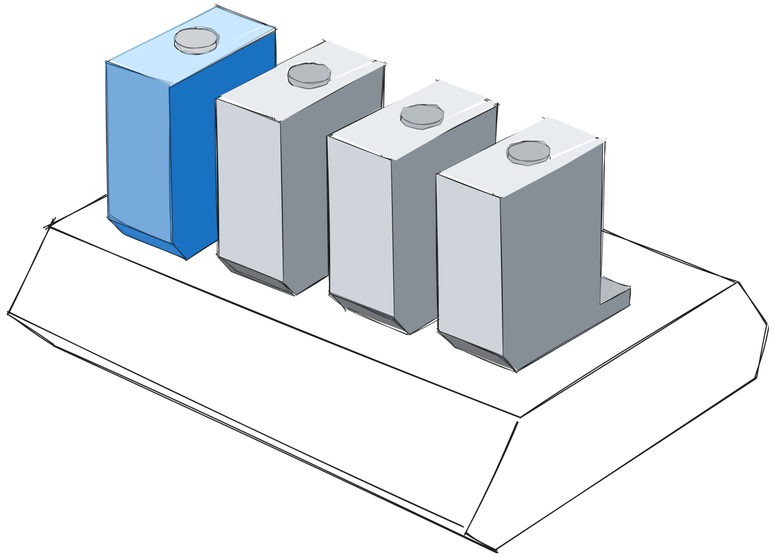
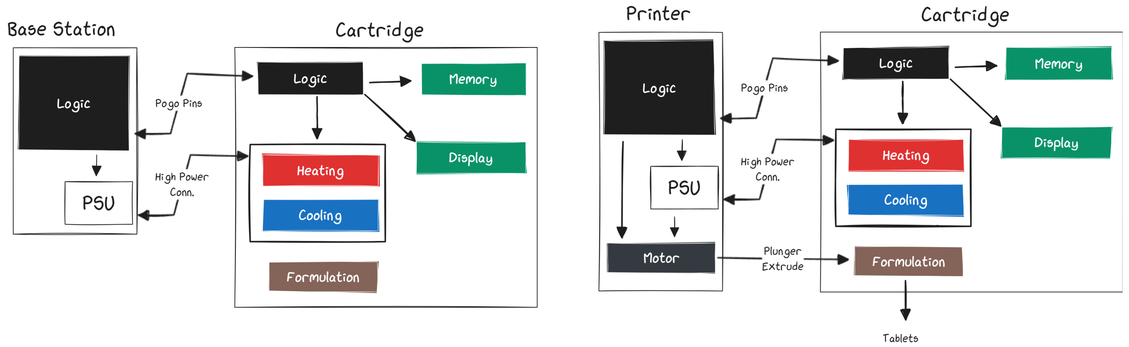
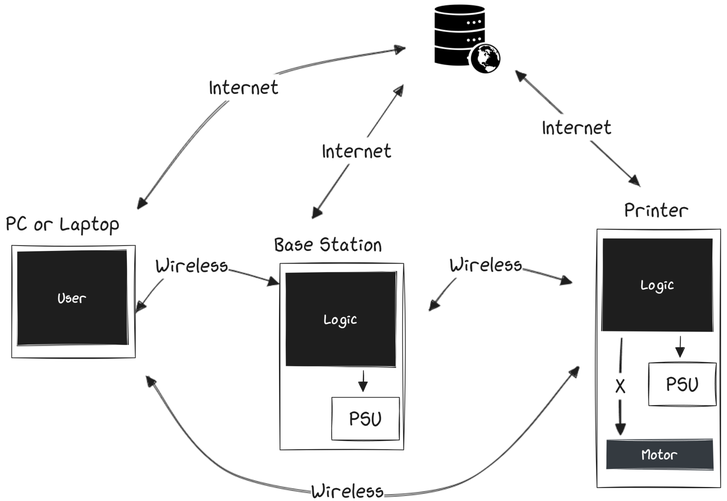


Figure 52 Base Station





printing processes. The Base Station connects to a laptop or computer, allowing pharmacists or researchers to configure the cartridge settings through an intuitive software interface. This setup enables precise control over the cartridge's internal environment, including heating, cooling, and material stabilization, ensuring that the formulation is in optimal condition before being transferred to the print head for actual printing.

The Base Station also leverages the smart capabilities of the Cartridge Plus, reading the onboard memory to access detailed information about the formulation, such as its composition, current temperature, and state (e.g., whether it is ready for printing or still undergoing preheating or cooling). Users can adjust settings remotely to fine-tune these conditions, ensuring that the formulation remains stable and ready for use at the right time.

Furthermore, the Base Station can update the cartridge's profiles and settings, preparing it for specific tasks based on the upcoming printing requirements. This process includes configuring custom temperature profiles, adjusting the material's viscosity, and ensuring that all necessary data is accurately recorded in the cartridge's memory module. This information is vital for maintaining consistency and quality in the printing process, as it ensures that each cartridge is fully prepared before being transferred to the printer.

Page Intentionally Left Blank

7. Evaluation

7.1 Feasibility of process

The feasibility of the cartridge-plus-ecosystem concept hinges on the new process. While the current process used by pharmacies is well-tested, I found no scientific literature confirming the stability of the new process.

To evaluate the feasibility of this new process (FIG. 46), it is essential to subject the formulations to thermal cycling and stress testing to ensure their integrity. To do this, I designed two experiments: the first involved thermal cycling the formulations for different durations, and the second involved rapidly solidifying them. Both tests were conducted on two formulations: one placebo and the other containing the active pharmaceutical ingredient

THANK YOU FOR YOUR INITIATIVE ON THESE TESTS. THEY'RE INVALUABLE, AS WE LACK STABILITY DATA. THIS COULD BE GROUNDBREAKING!

– DOSER

Setup 1: Formulation Preheating and Reuse:

I constructed a climate chamber for this setup, housing four cartridges. Each cartridge was equipped with a temperature sensor, specifically an NTC thermistor 10K MF52AT, to monitor temperatures. The cartridges were wrapped in silicone heater mats for heating and insulated with XPS foam to minimize heat loss, creating a controlled environment. Heating was regulated by an ITSY BITSY M4 micro-controller running Circuit Python v9.0.2, which was connected to four MOSFETs for individual control of the heater mats. The temperature sensors were monitored at a frequency of 10 Hz.

Three different heating regimens were established for the cartridges, with the fourth cartridge serving as a control. The heating and cooling durations for the three cartridges were based on potential use scenarios derived from interviews and observations of end users.

Setup 2: Formulation Rapid Solidifying

This experiment was conducted using two cartridges. Two beakers were prepared: one filled with ice-cold water maintained at 0°C, and the other with tap water maintained at 19°C. Thermometers were used to continuously monitor the temperature in each beaker. To prevent water from entering the cartridges, they were wrapped in chemically inert nitrite gloves. The cartridges were then filled with formulations and immersed in the beakers for two hours before being printed. A third control cartridge was prepared and printed according to the standard operating procedure (SOP).

Results:

The tablets were round, displaying exceptional quality and uniformity on their surfaces, which suggested an absence of defects and strong layer integrity. In the preheating experiment , the placebo tablets were white, while those containing the API had a slight yellow tint. This yellowing was more pronounced in the tablets subjected to the 8-hour and continuous cycles, possibly indicating thermal degradation.

There was very low weight difference between batches, with all printed tablets showing a relative standard deviation (RSD) of ≤ 4.0%, in compliance with regulatory standards. Content uniformity analysis was performed on the 3D-printed tablets to confirm that the active pharmaceutical ingredient (API) was evenly distributed within them. The HPLC (High Performance Liquid Chromatography) analysis results demonstrated excellent content uniformity according to USP (United States Pharmacopoeia Convention, 2011) criteria (90%-110%).

Conclusions:

This study introduces a disruptive approach to pharmaceutical manufacturing by validating the technological advancements of the new heating and cooling process. The findings demonstrate that these thermal cycles do not compromise the quality of the final printed tablets, ensuring that formulations within the cartridges remain stable and robust even after multiple reuses. This stability under thermal stress marks a significant improvement in the reliability of pharmaceutical production.

Moreover, the study investigates the feasibility of using stainless steel cartridges as a sustainable alternative to traditional methods. By simulating commercial conditions, the research highlights the potential of these reusable cartridges to withstand operational stresses, thereby offering a more sustainable and efficient solution for formulation development.

The results suggest, that this innovative approach could transform the field by enhancing both the efficiency and environmental sustainability of pharmaceutical manufacturing. This new method not only optimizes the production process but also sets a precedent for future research and development, potentially leading to widespread adoption and significant industry-wide impact.

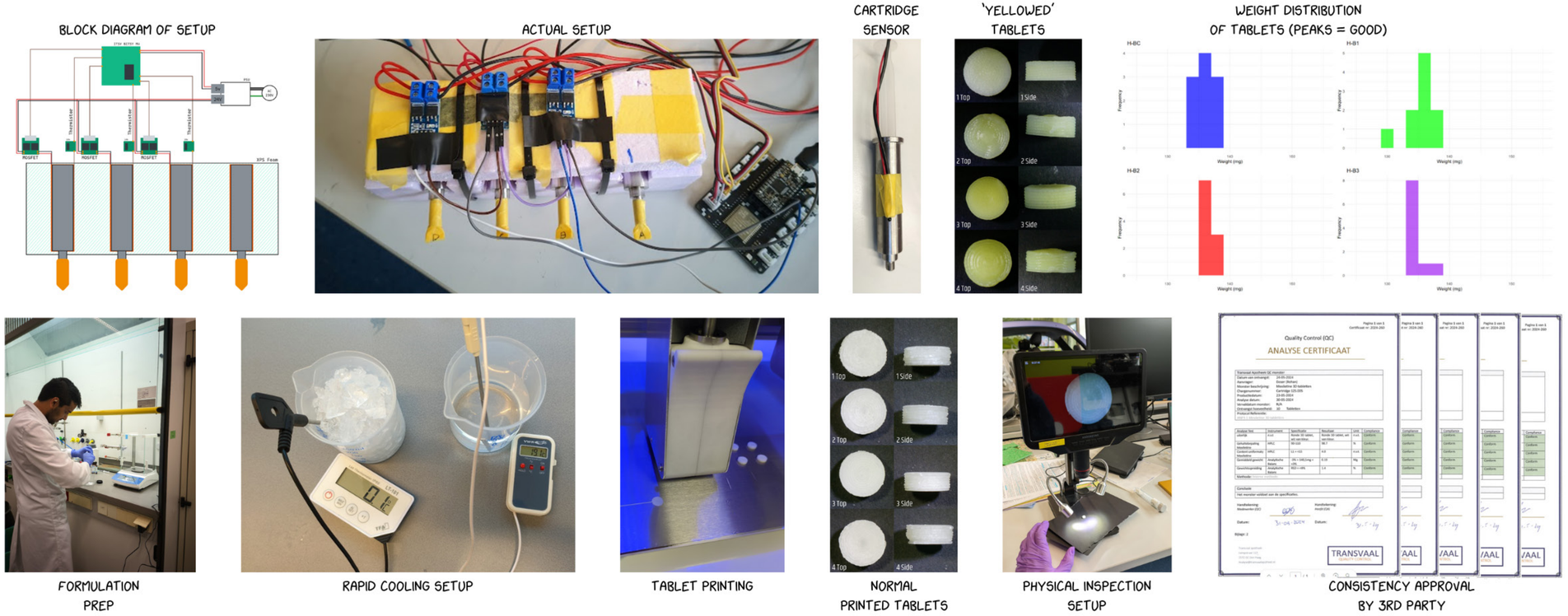


Figure 53 Overview of Heating and Cooling

7.2 Feasability of Peltier Module

Note: Doser has requested to keep nozzle heating is out of scope for this thesis

The second key aspect of this new concept is integrating a Peltier module to heat and cool the cartridges within the same unit. A feasible process is of little value if it cannot be implemented commercially. My proposed design incorporates a Peltier module for both rapid solidification and preheating of the formulations.

A Peltier module consists of two types of semiconductor elements arranged between copper substrates. When electricity flows through the module, electrons move through one element while positive holes move through the other—a phenomenon known as the “Peltier effect.” This causes one side of the substrate to absorb heat and the other to emit it, allowing the hot and cold sides to switch depending on the direction of the current. The module can also function as a thermoelectric generator through the “Seebeck effect,” where a current is generated by applying a temperature difference across the module (Peltier Module - KYOCERA, n.d.).

As previously discussed in section 4, uniform heating of the formulation is critical. Doser’s current solution successfully addresses this requirement. However, integrating the Peltier module into this system presents a challenge due to its geometry. The Peltier module is typically manufactured in flat shapes, coated with ceramic. This rigid module cannot efficiently transfer heat to and from the cylindrical cartridge. To overcome this, I have designed a heat sleeve. This component serves as an intermediary between the flat Peltier module and the curved cartridge surface. The heat sleeve’s primary function is to efficiently transfer heat from the planar hot side of the Peltier module to the cylindrical surface area of the cartridge.

Study:
A simulation was conducted to analyze the heat flux and temperature gradient from the cartridge body to the side of the Peltier module

Results:

As illustrated in the simulation (Fig. 54), the heat sleeve exhibits negligible thermal resistance, allowing it to be disregarded in subsequent calculation.

Heat Sink Estimation (Fig. 55)
The total thermal energy required to cool a cartridge filled with the formulation from 80°C to 0°C is 1229.12 J.

To achieve cooling within 20 minutes, the required cooling power is calculated as 1229.12 J / (20 × 60 s) = 1.024 W.

Assuming a Peltier module efficiency of 10%, the total power on the hot side of the Peltier module is calculated to be 1.024 W + 1.024 W / 0.10, which is approximately 11 W.

To dissipate 11 W of power at 50°C (the lowest temperature on the Peltier’s hot side), a heat sink with dimensions of 70 × 30 × 25 mm is required (Heat Sink Calculator | Celsia, 2020). These dimensions are comparable to those of NVMe drive heat sinks, which are designed to cool PC hard drives with similar power requirements.

Conclusion:
While these preliminary calculations suggest that the heating system is feasible, they are based on rough estimates. More detailed calculations are necessary to accurately design a custom heat sink that optimizes the overall system size

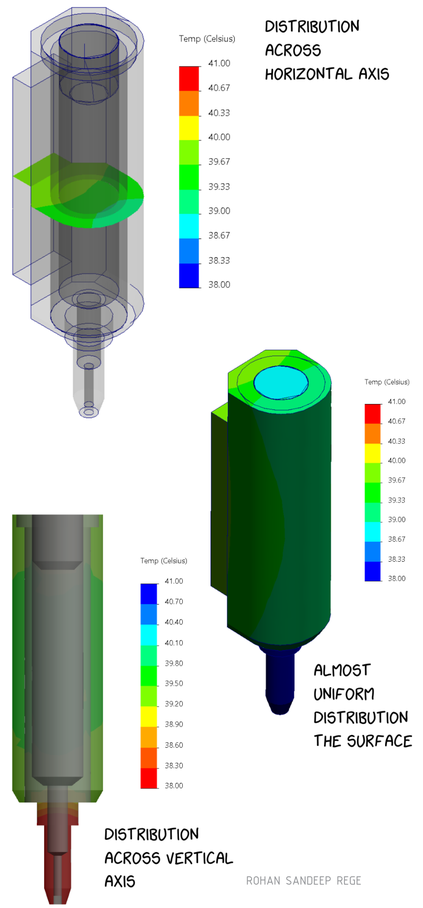
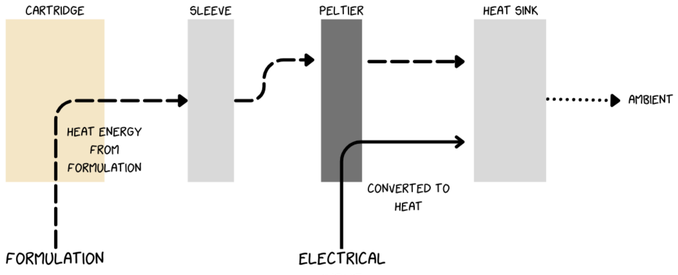


Figure 54 Simulations



Heating energy (formulation):
$Q = m \cdot c \cdot \Delta T$
Where:
- 0.0068 kg (mass of the formulation calculated from density provided by Doser)
- c=2260 J/(kg·°C) (specific heat capacity of the formulation provided by Doser)
- ΔT=80−0 °C (temperature change 80 to 0)

$Q = 0.0068 \times 2260 \times 80$
$Q = 1229.12$ J

The cooling rate required:
$Pc = Q/t$
$Pc = 1229.12 / (20 \times 60)$
$Pc = 1.024$ W

Peltier Electrical energy required:
Efficiency (η) = 10%
$Pp = Pc/\eta$
$Pp = 10.24$ W

Total Power:

$P = Pp + Pc$
$P = 11$ W (approx)

Heat Sink Sizing Calculator - Rough Estimate

Estimate the overall volume of the heat sink required to cool a heat source by using the following equation:

V= (Q*Rv)/Delta T

Heat sink volume in cm^3 = (heat source power in watts x volumetric thermal resistance) / (Tjunction - maximum ambient temperature)

Inputs (in yellow)

Heat Source Power (Q)	11.0	Watt
Tcase Max (manuf supplied)	50.0	Deg. C
Max Ambient Temperature	19.0	Deg. C
Delta - T (Thermal Budget)	31.0	Deg. C
Volumetric Thermal Resistance (Rv)	150.0	
(refer to table at right)		
Estimated Heat Sink Volume	**53.2**	**cm^3**

Air Flow	Properties	Volumetric Thermal Resistance
Natural Convection	Little to no air / no noise	Rv = 500 - 800
1.0 m/s ~200 lfm	Gentle air, very low noise	Rv = 150 - 250
2.5 m/s ~500 lfm	Moderate air	Rv = 80 - 150
5.0 m/s ~1,000 lfm	Fast, loud air	Rv = 50 - 80

1. Smaller heat sinks of 100-200 cm^3 use values in the lower Rv range.
2. Larger heat sinks of 1,000 cm^3 use values in the upper RV range.
3. Actual thermal resistance values may vary outside range based on several factors.
4. Model assumes fin design is optimized for a given air flow.

Desired Heat Sink Volume

Length	7.0	cm
Width	3.0	cm
Height (base plus fin)	2.5	cm
Desired Heat Sink Volume	**52.5**	**cm^3**

Your Desired Heat Sink Size is **0.7** **cm3 smaller than required**

Reference
https://www.electronics-cooling.com/1995/06/how-to-select-a-heat-sink/

Figure 55 Heaksink Estimation

7.3 Viability of the System

Autonomy of Pharmacies:

The Cartridge Plus ecosystem represents a significant advancement in preserving and enhancing the autonomy of pharmacies. Currently, pharmacies are limited by the time-consuming process of refilling cartridges, eventually leading them to rely on third-party vendors for prefilled formulations. This dependency threatens to erode their independence over time. Something that they strive for.

With Cartridge Plus, pharmacies can refill cartridges on-site efficiently, maintaining control over their operations. This system allows pharmacists to continue tailoring formulations to patient-specific needs, such as modifying excipients based on allergies, thereby upholding the same standards in patient care. Moreover, pharmacies can sustain their traditional role in patient relationships and community healthcare by compounding their formulations.

> PHARMACISTS CAN DO CARTRIDGE FILLING THEMSELVES AND REFILL THEM, I WOULD SAY IT IS A USP FOR DOSER, IT CREATES FLEXIBILITY FOR THE CLIENT.
>
> – CEO, DOSER

Increase in Productivity:

The Cartridge Plus ecosystem significantly enhances productivity by streamlining the entire process, from mixing formulations to printing tablets. This innovation reduces the time required for these tasks, allowing pharmacies to produce more tablets daily and serve more patients. For researchers, this increase in efficiency accelerates the pace of scientific inquiry.

The management console system also provides an overview of the printer and process, including real-time status updates on formulations and inventory.

The automation enabled by this design concept

minimises human error and variability, leading to more precise and consistent tablet production. The modular design of the cartridges further reduces downtime, as faulty cartridges can be easily replaced, ensuring continuous operation. This advancement not only boosts productivity but also supports the sustainability of pharmacy operations by optimising resource use.

Environmental and Social Impact:

The Cartridge Plus ecosystem also offers significant environmental benefits. Encouraging pharmacies to refill cartridges in-house dramatically reduces the need to ship prefilled cartridges from vendors, resulting in lower carbon emissions associated with transportation and packaging. This shift supports a more sustainable approach to pharmaceutical distribution.

Socially, the system empowers smaller pharmacies by reducing their dependency on large suppliers, enabling them to remain competitive and maintain their autonomy in the market. It also ensures that patients can continue receiving personalised care, such as the ability to modify excipients based on individual needs.

Benefits for Doser:

The Cartridge Plus ecosystem expands Doser's capabilities by increasing the number of tablets that can be printed daily. Additionally, it opens up new avenues for revenue generation by broadening Doser's product and service offerings, which can be monetised. This diversification enhances Doser's market position.

Looking ahead, the 3D-printed tablet market is poised to attract formulation developers by providing them with the tools to create specific profiles for their materials. This capability ensures that formulations are printed with precise settings, guaranteeing compliance with regulatory standards. For regulators, this system offers greater oversight and confidence in the consistency and safety of pharmaceutical products. As a result, the ecosystem encourages the development of new formulations, fostering innovation within a quality control framework.

7.4 Desirability

The Cartridge Plus ecosystem not only maintains the existing printing speed but enhances efficiency by allowing multiple formulations to be kept ready for immediate use, reducing downtime and increasing productivity. By automating the solidifying and preheating processes, the system significantly decreases the printer's cycle time, eliminating the need for pharmacists to monitor the process continuously. This automation not only streamlines operations but also fits seamlessly into the structured workflows of commercial pharmacists while remaining adaptable enough to support the more flexible requirements of researchers.

The system's ability to automate routine tasks reduces variability in the printing process, leading to more precise and consistent results. This means pharmacists spend less time reprinting due to errors, allowing commercial pharmacies to deliver medications faster with fewer human resources. Furthermore, the Cartridge Plus acts as a material passport, providing clear, accessible information about the contents and status of each cartridge, which is especially useful for tracking formulations in storage and during use. This feature also aids quality control teams by simplifying the detection and reporting of deviations, ultimately improving overall product quality. It also means easier audits by regulatory bodies.

> IF YOU MAKE THE PROTOTYPE, WE WANT TO TEST IT. WE MIGHT JUST KEEP IT WITH US. HAHA!
>
> – DOSER'S CLIENT

By creating a system that reduces human intervention and increases reliability, the Cartridge Plus ecosystem offers new value to stakeholders, particularly by encouraging pharmacies to create and print their formulations with greater ease and confidence. Additionally, it stimulates formulation vendors to adopt this technology by having higher compliance within the pharmaceutical manufacturing process.

On a broader scale, the Cartridge Plus ecosystem could significantly impact the pharmaceutical domain by setting new standards for efficiency, flexibility, and quality control, ultimately benefiting individual stakeholders, the industry, and society.

8 Conclusions

8.1 Research Problem

The initial assignment provided by Doser evolved significantly as the project progressed. While Doser correctly identified a preliminary issue, further research revealed the need for a more in-depth exploration. This process involved extensive engagement with a diverse range of stakeholders, including users, clients, and end-customers, to identify the underlying or latent problems that were not immediately obvious. Through these interviews and interactions, it became evident that the problem was more complex than initially perceived.

As a result, the original problem statement was re-assessed and refined, leading to the development of a more precise and relevant research question. This iterative process was crucial in ensuring that the project targeted the core issues, ultimately guiding the research and development towards solutions that are both meaningful and impactful. The modification of the problem statement and the formulation of a new research question were essential in aligning the project with the genuine needs and expectations of all stakeholders.

The thesis now addresses the following research questions:

RQ1: What are the use cases and contexts for the Rx1 printer’s application?

RQ2: What are the critical variables in the Rx1 printing procedure? And how do we optimise them?

RQ3: What are the specific end-user requirements for the Rx1 across different operational contexts?

8.2 Method

To address the first and third research questions, I primarily employed ethnographic studies and interviews, drawing from the Creative Problem Solving (CPS) method as outlined by Van Boeijen et al. (2014). This approach allowed for a deep exploration of the end-user’s environment, behaviors, and needs. By immersing myself in the users’ contexts and engaging in direct conversations, I gained a comprehensive understanding of

the various challenges they face, as well as their expectations from the Rx1 printer. These insights were crucial in identifying the nuanced and often unspoken issues that affect the usability and effectiveness of the printer in real-world scenarios.

For the second research question, which required a more technical approach, I utilized methods rooted in creative facilitation and the iCPS framework (Boom, 2019). Techniques such as TRIZ 40 and brainwriting were particularly valuable in dissecting the problem and managing its complexity. TRIZ 40, for example, helped in identifying and prioritizing the critical variables within the Rx1 printing procedure by simulating various stress scenarios. Brainwriting, on the other hand, facilitated the generation of a wide range of ideas and potential solutions by encouraging collaborative creativity in a structured manner. These methods were instrumental in breaking down the technical challenges into manageable components, enabling a more systematic and thorough exploration of the Rx1 printer's operational intricacies.

Together, these methodologies provided a robust framework for understanding and addressing the multifaceted problems associated with the Rx1 printer, ensuring that the solutions developed were both user-centric and technically sound.

8.3 Key Findings

The printer, marketed by Doser primarily as a printing device, is actually utilized by users for a broader range of functions, akin to a multifunctional device that performs printing, copying, and scanning tasks. This discrepancy between the marketed use and actual usage is the one of the cause of the problem.

A key finding from the study was that, although preheating the printer does require time, it is not the most significant time-consuming factor in the overall process. The most time-intensive stage is the complete drying and solidification of the formulation within the cartridge. Small operational issues, such as improper bed leveling and inadequate preheating, while individually not excessively time-consuming, collectively contribute to delays and can cause considerable mental stress for the users.

For certain formulations, it is possible to rapidly solidify them and use them immediately for printing. Similarly, some formulations can endure extended preheating periods, although this may lead to some degree of degradation.

These findings suggest that while the printer's current operational processes are functional, there is room for optimization, particularly in reducing the time and stress associated with the preparation stages of printing. This also points to the need for a more nuanced understanding of compounding practices, tailored to the specific needs and expectations of various stakeholders.

8.5 Limitations and Recommendations

Limited Scope on Client Interaction:

Due to constraints in availability, I was only able to engage with three clients. While I conducted multiple interviews with different individuals within each client organization, having access to a more diverse user base would have been beneficial. A broader range of participants could have provided additional context and insights, potentially revealing a wider array of requirements and enhancing the overall understanding of user needs.

Limited Scope on Formulation Testing:

The stability tests conducted during this study were limited to only a few formulations. Given that pharmacopoeias, such as the European Pharmacopoeia (Phr. EU, 2023), include thousands of formulations, a broader testing scope would have been advantageous. Evaluating a more extensive range of formulations, particularly those with similar excipients or from the same category, could have provided valuable insights and allowed for more comprehensive comparisons. This expanded testing could have facilitated a deeper understanding of formulation stability and performance across different contexts.

Limited Scope on Design:

Due to the extended duration required for the research phase, there was insufficient time

to fully develop and embody the design. As a result, while the concept has been validated, it remains in a conceptual stage and has not yet been fully refined for manufacturability. This limitation means that the design has not been fully realized in practical terms, which impacts its readiness for production and implementation.

-fin-

9 References

Boom. (2019, April 3). Road Map for Creative Problem Solving Techniques. https://www-boom-nl.tudelft.idm.oclc.org/hoger-onderwijs/100-8535_Road-Map-for-Creative-Problem-Solving-Techniques

CE marking – obtaining the certificate, EU requirements - Your Europe. (n.d.). Your Europe. https://europa.eu/youreurope/business/product-requirements/labels-markings/ce-marking/index_en.htm

Delft Design Guide. (2020, February 24)

Desmet, P. M. A., Hekkert, P., & Desmet and Hekkert. (2007). Framework of Product Experience. In International Journal of Design (Vol. 1, Issue 1, pp. 13–23) [Journal-article]. https://diopd.org/wp-content/uploads/2012/02/frameworkproductex.pdf

Developing Solid Oral Dosage Forms. (n.d.). ScienceDirect. https://www.sciencedirect.com/book/9780128024478/developing-solid-oral-dosage-forms

Doser. (2024, March 14). Homepage - Doser. https://dosermedical.com/

J3400_202312: NACS Electric Vehicle Coupler - SAE International. (n.d.). https://www-sae-org.tudelft.idm.oclc.org/standards/content/j3400_202312/

Javaid, M., Haleem, A., Singh, R. P., & Suman, R. (2021). Substantial capabilities of robotics in enhancing industry 4.0 implementation. Cognitive Robotics, 1, 58–75. https://doi.org/10.1016/j.cogr.2021.06.001

JUMBO paracetamol 500 mg, tabletten | Geneesmiddeleninformatiebank | College ter Beoordeling van Geneesmiddelen. (n.d.). https://www.geneesmiddeleninformatiebank.nl/nl/rvg112988

López-Vidal, L., Real, J. P., Real, D. A., Camacho, N., Kogan, M. J., Paredes, A. J., & Palma, S. D. (2022). Nanocrystal-based 3D-printed tablets:

Semi-solid extrusion using melting solidification printing process (MESO-PP) for oral administration of poorly soluble drugs. International Journal of Pharmaceutics, 611, 121311. https://doi.org/10.1016/j.ijpharm.2021.121311

Mugge, R., Govers, P. C., & Schoormans, J. P. (2009). The development and testing of a product personality scale. Design Studies, 30(3), 287–302. https://doi.org/10.1016/j.destud.2008.10.002

Patton, M. Q. (2002). Two decades of developments in qualitative inquiry. In Qualitative social work (Vol. 4, Issue 3, pp. 261–283). https://uk-sagepub-com.tudelft.idm.oclc.org/en-gb/eur/qualitative-research-evaluation-methods/book232962

Peltier module (Thermoelectric module) - Energy Conversion Devices - KYOCERA. (n.d.). KYOCERA GROUP GLOBAL SITE. https://global.kyocera.com/prdct/ecd/peltier/

Personalized Medicine Market Size, Share & Trends Analysis Report By Product (Personalized Medicine Diagnostics, Personalized Medicine Therapeutics), By End-use, By Region, And Segment Forecasts, 2024 - 2030. (n.d.). https://www.grandviewresearch.com/industry-analysis/personalized-medicine-market

Piccola Tablet Press – Riva Europe. (n.d.). https://riva-europe.co.uk/products/piccola-tablet-press

Rapaille, A., Goosens, J., & Heume, M. (2003). SUGAR ALCOHOLS. In Elsevier eBooks (pp. 5665–5671). https://doi.org/10.1016/b0-12-227055-x/01164-0

Research, P. (2024, February 1). Personalized Medicine Market Size to Hit USD 1,233.23 Billion by 2033. https://www.precedenceresearch.com/personalized-medicine-market

Rieder, M. (2019). Adverse Drug Reactions in Children: Pediatric Pharmacy and Drug Safety. □the □Journal of Pediatric Pharmacology and Therapeutics, 24(1), 4–9. https://doi.org/10.5863/1551-6776-24.1.4

Seoane-Viaño, I., Januskaite, P., Álvarez-Lorenzo, C., Basit, A. W., & Goyanes, Á. (2021). Semi-solid extrusion 3D printing in drug delivery and biomedicine: Personalised solutions for healthcare challenges. Journal of Controlled Release, 332, 367–389. https://doi.org/10.1016/j.jconrel.2021.02.027

Sidhu, P., Papalois, V., Anderson, D., Michaelides, D., Von Eiff, W., Kumar, N., Rohr-Kirchgraber, T., Henke, N., Bartlett, R., Ramsay, M., Thompson, L., Frejd, A., Meyenburg-Altwarg, I., Lega, F., Rassaf, T., Pritchard, D., Räsänen, I., Sinipuro, J., Parra-Calderón, C., . . . Kaminskiy, D. (2019). Leadership • Cross-CoLLaboration • Winning praCtiCes. EUROSON 2019, 19(3). https://healthmanagement.org/uploads/article_attachment/hm-v19-i3-infographic.pdf

Statista. (n.d.). Pharmaceuticals - Worldwide | Statista Market Forecast. https://www-statista-com.tudelft.idm.oclc.org/outlook/hmo/pharmaceuticals/worldwide?currency=EUR

Statista. (2021, October 19). Global precision medicine market size by application 2017. https://www.statista.com/statistics/1010458/precision-medicine-market-size-worldwide-by-application/

Tassoul, M. (2009). Creative facilitation.

The Growing Role of Precision and Personalized Medicine for Cancer Treatment. (2019, January 28). World Scientific Publishing. https://www.worldscientific.com/page/pressroom/2019-01-28-01

Tools of the Trade | RPS. (n.d.). https://www.rpharms.com/about-us/museum/explore-the-collection/tools-of-the-trade

United States Pharmacopeial Convention. (2011). Stage 6 Harmonization. In United States Pharmacopeial Convention. https://www.usp.org/sites/default/files/usp/document/harmonization/gen-method/stage_6_monograph_25_feb_2011.pdf

Vreeman, G., & Sun, C. C. (2022). Air entrapment during tablet compression – Diagnosis, impact on tableting performance, and mitigation strategies. International Journal of Pharmaceutics, 615, 121514. https://doi.org/10.1016/j.ijpharm.2022.121514

Wang, S., Chen, X., Han, X., Hong, X., Li, X., Zhang, H., Li, M., Wang, Z., & Zheng, A. (2023). A Review of 3D Printing Technology in Pharmaceutics: Technology and Applications, Now and Future. Pharmaceutics, 15(2), 416. https://doi.org/10.3390/pharmaceutics15020416

WEEE - what does the label mean, EU requirements - Your Europe. (n.d.). Your Europe. https://europa.eu/youreurope/business/product-requirements/labels-markings/weee-label/index_en.htm

Ztl, S. (2024, March 26). Top 6 Medical-Grade Materials You Should Know. Zintilon. https://www.zintilon.com/blog/top-6-medical-grade-materials/